# ELEMENTARY HUMAN PHYSIOLOGY

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# NOTES OF LECTURES

ON

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# HUMAN PHYSIOLOGY

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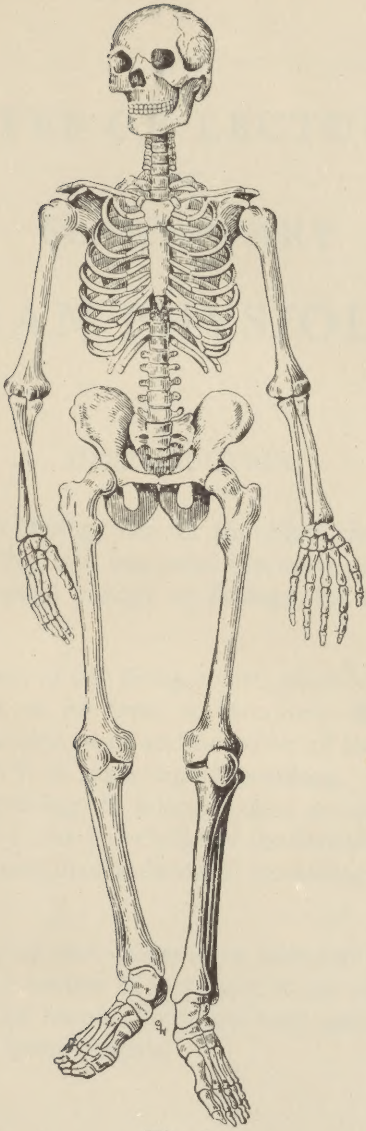

Fig. 1

# NOTES OF LECTURES

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# HUMAN PHYSIOLOGY

## INTRODUCTION

The science of **Biology** has for its object the study of living things. It is divided into two great branches—vegetable biology or **Botany** and animal biology or **Zoology,** for plants as well as animals are alive.

Further, the study of any living object, plant or animal, includes a knowledge first of its form or structure—**Morphology**—and second of the functions, uses and activities of the various organs or parts of which it is made up—**Physiology.** Morphology, or anatomy, and physiology to a large extent go hand in hand, for, in order to obtain a true knowledge of the functions of any organ or organism, we must first understand something about its structure or anatomy.

The physiology of man differs in no essential from that of the lower animals; as a matter of fact most of our real knowledge of the functions of the human body has been gained from experimental studies on lower animals.

## STRUCTURE OF HUMAN BODY

As we shall see later, all the tissues of the body are derived from a single cell, the fertilized ovum. In the process of development differentiation of structure is accompanied by specialization of function, and the higher we go in the animal scale the more complex does the organism become, both in its anatomy and physiology. Probably no mechanism we know of approaches the human body in complexity of structure and function.

Each part of the body having a special function of its own to perform is termed an **Organ,** e. g. stomach, liver, brain, etc.

Groups of organs related in function are termed **Systems;** for example, each individual muscle is an organ, but all muscles, of whatever variety, have a common function, viz.—to produce movement of some kind or other, and so together they form the muscular system. The heart and the blood vessels (arteries, capillaries, veins), together with the lymphatics, are concerned with the continuous movement of the blood in a circle, and so form the circulatory system, etc.

The body may be regarded as consisting of the following systems,—

**Skeletal System** consists of bones, cartilages and ligaments.

**Muscular System**—Muscles whose function it is to shorten or contract and so to produce movement.

**Nervous System**—Brain and spinal cord, cranial and spinal nerves, etc.

**Circulatory System**—Heart, bloodvessels and lymphatics.

**Respiratory System**—Air passages, windpipe and larynx, lungs, muscles of respiration.

**Alimentary System**—Stomach, intestine, liver, pancreas, etc.

**Endocrinous System**—Glands producing internal secretions such as suprarenal capsules, thyroid, parathyroids, pituitary, reproductive glands, pancreas, etc.

**Excretory System**—Skin, kidneys, liver, lungs.

**Reproductive System**—Ovaries, testes, male and female organs of generation.

When the different organs are examined by the microscope it is seen that all are made up of textures or **tissues** which consist of **Cells, Intercellular substance** and **Fibers;** therefore, the ultimate analysis shows the body to be composed of microscopic units termed cells, with intercellular substance and fibers derived from them.

# THE TISSUES OF THE BODY

The important discoveries of Schleiden (1838) and Schwann (1839) showed that the tissues of plants and animals are not continuous structures, but are made up of small units, of microscopic size, termed cells. The unit in biology, is the cell just as in chemistry it is the atom and in physics the electron.

**Structure of Typical Animal Cell**—The cell in the human body may vary from 1/300 to 1/3000 of an inch in diameter. It consists of three portions, the **cell protoplasm,** the **nucleus,** and the **centrosome and attraction sphere.**

1. **The Cell Protoplasm or Cytoplasm** is a soft-jelly-like material consisting of a dense network of fibrillæ termed the **spongioplasm,** with a more fluid portion in its meshes called the **hyaloplasm.** The hyaloplasm may contain true **granules** and **vacuoles,** but the intersections of the spongioplasmic network often, under the microscope, present a granular appearance. The whole may or may not be surrounded by a definite **cell membrane.**

2. **The Nucleus** is generally round or oval and usually occupies a position not far from the center of the cell. It is enclosed in a distinct envelope, the **nuclear membrane.** The contents of this membrane, like the cell protoplasm, consist of a network of coarse threads which readily stain with dyes and on this account is called the **chromoplasm;** it corresponds to the spongioplasm of the cell body, the strands of the nuclear network, however, being much coarser. The interstices of this spongework are filled with a more fluid, non-staining material termed the nuclear sap or **nuclear hyaloplasm.** A rounded, denser portion of the chromatin material, found somewhere within the nucleus, is called the **nucleolus;** there may be more than one.

3. **The Centrosome with its Attraction Sphere** is situated in the cell protoplasm, near the nucleus. The former is a minute particle which appears to have an attractive influence on the protoplasmic fibrils and granules in its neighborhood, this giving rise to what is known as the **attraction sphere.** The centrosome initiates the complicated process of cell division known as **mitosis** or **karyokinesis.**

The nucleus has an important influence on the nutrition of the cell body; ANY PART OF THE CELL PROTOPLASM WHICH IS CUT OFF FROM THE NUCLEUS UNDERGOES DEGENERATION.

## PROTOPLASM

Protoplasm was called by Huxley the "physical basis of life" since it enters into the composition of every living tissue. It is a viscous and, usually, colorless substance, neutral or slightly alkaline in reaction.

**The Chemical Composition** of living protoplasm is unknown since any attempt at analysis must necessarily kill it. The analysis of dead protoplasm shows that it contains at least 75% of water and 25% or less of solids. The solids consist of **organic** (protein essential) and **inorganic** constituents, and ultimate analysis shows that the human body contains the following chemical elements: **Carbon, oxygen, hydrogen, nitrogen,** sulphur, phosphorus, iron, sodium, potassium, lithium, calcium, magnesium, manganese, chlorine, fluorine, iodine, and silicon; several of these exist only in traces.

### Vital Properties of Protoplasm

1. **Power of Assimilation and Disassimilation**—In living protoplasm certain chemical changes are always going on. It has the power of building up into its own substance materials taken in from the outside in the form of food; at the same time disintegrative changes are taking place in it whereby large and complex molecules are being broken down into simpler ones, which are finally excreted. The first of these processes is termed **assimilation** or **anabolism** (upbuilding), the second **disassimilation** or **katabolism** (downbreaking), and the term **metabolism** is used to include the sum total of all these chemical rearrangements.

In the child the anabolic changes predominate and growth takes place; in starvation, wasting disease and old age the katabolic changes are in excess, and the body loses weight, while in the healthy adult, where the body weight does not change appreciably, the two balance each other.

No inorganic or dead substance that we know of possesses this property.

2. **Excitability or Irritability**—Living protoplasm is excitable or irritable, and by this is meant that it has the power of responding to stimulation or irritation applied from the outside.

Changes in the surroundings may either attract or repel the protoplasm. Such attraction or repulsion may be caused by various chemical substances (**chemiotaxis**), by mechanical pressure (**barotaxis**), by light (**phototaxis**), by changes in temperature (**thermotaxis**) and by electricity (**galvanotaxis**).

If the reaction is toward the stimulus it is said to be **positive,** and if away from it **negative;** thus we may have positive or negative chemiotaxis according as the protoplasm is attracted or repelled by the chemical substance, etc. A good example of positive chem-

iotaxis is seen in the movement of the white blood corpuscles towards the various microbes, or other foreign bodies, which may enter the tissues.

Certain unicellular organisms, particularly plant cells, are attracted by light—positive phototaxis, and others are repelled by it—negative phototaxis, while some of the infusoria when brought between the poles of a glavanic battery may be seen to move towards the positive pole and others towards the negative pole.

These phenomena explain the apparently voluntary movements of many unicellular organisms which, for example, appear to select certain kinds of food while in reality they are compelled to move towards it by chemical attraction. The apparently spontaneous, **amœboid movement** of white blood corpuscles is probably the result of chemiotaxis.

3. **Reproduction.** Living protoplasm has the property of reproducing itself. Cells, when they reach a certain size, either divide to form two smaller cells, or die and disappear.

Cell division may either be **direct** or **indirect.** The latter method, termed **mitosis** or **karyokinesis,** is much the more common, and is a very complicated process. It appears to be INITIATED BY THE CENTROSOME AND THE NUCLEUS which in dividing passes through a series of remarkable changes a detailed description of which will be found in any work on histology.

In **amitotic or direct cell division,** which is rare, the cell protoplasm and nucleus divide into two parts directly, without any preliminary changes in the centrosome and nucleus. The result, as in mitotic division, is the production of two daughter cells from one original mother cell.

The cause of cell division is not understood, but it may possibly be due to defective nutrition. As any spheroidal body grows bigger, the volume or mass increases more rapidly than the surface, hence as the cell becomes larger and larger, the surface, which represents the feeding area, becomes smaller and smaller in relation to the mass of material to be nourished, and something of the nature of starvation of the cell protoplasm may take place. The alterations in the metabolism, so induced, may set up the changes in the nucleus and centrosome which lead to the division of the cell.

**The Ovum is a Typical Cell**—All the tissues of the body are derived from the impregnated ovum.

After union of male and female pronuclei to form nucleus of fertilized ovum, the cell (ovum) divides by mitosis into two daughter cells, then each of these into two, making four, and so on until, in the young embryo, three layers of cells are formed termed **epiblast** or **ectoderm** (outer layer), **hypoblast** or **entoderm** (inner layer) and **mesoblast** or **mesoderm** (middle layer).

**Tissues derived from ectoderm**—Epidermis (scarf-skin) and its derivatives, nail, hair, epithelium of sebaceous, sweat and mammary glands; epithelium of mouth and nose; brain, spinal cord, nerves and ganglia; parts of eye and ear.

**From Entoderm**—Epithelium of pharynx, gullet, stomach, small and large intestine, pancreas, liver and gall bladder; epithelium of larynx, windpipe, lungs, and of thryoid and parathyroid glands; epithelium of urethra and urinary bladder.

**From Mesoderm**—All the other tissues of the body, including connective tissues (bone, cartilage, etc.) muscles, blood-vessels, heart, etc.

All tissues are composed of **cells, intercellular substance and fibers.**

Amount of intercellular substance varies in different tissues; ground substance (in cartilage) cement substance (in endothelium).

In process of development from original cell great specialization in structure and function takes place.

Tissues may be arranged into five great groups,—EPITHELIUM, CONNECTIVE TISSUES, MUSCLE, NERVE, BLOOD AND LYMPH.

## I. EPITHELIAL TISSUES

Cells are arranged on free surfaces. Varieties:

1. **Simple Squamous or Pavement Epithelium**—Flat nucleated cells united at margins by cement substance, forming a single layer. Outlines shown by treatment with silver nitrate.

Found lining the great serous cavities (pericardial, pleural, peritoneal), heart, blood-vessels and lymphatics. Here frequently termed ENDOTHELIUM, where it forms a smooth frictionless surface. Also lines air cells of lungs and covers posterior surface of cornea and anterior surface of iris.

2. **Stratified Squamous Epithelium**—Several layers or strata of cells.

Found in epidermis of skin; lining mouth, nose, pharynx, gullet; covering conjunctiva and anterior surface of cornea.

Has mainly a protective function.

Surface cells have lost their nuclei and become transformed into a horny substance termed KERATIN, impervious to water. They are dead and are continually being shed and replaced by cells from deeper layers.

3. **Transitional Epithelium** is really a special form of stratified squamous epithelium. Lines ureters, urinary bladder and part of urethra.

4. **Columnar Epithelium**—So called because cells are shaped like columns.

Found lining stomach, small and large intestine, ducts of glands opening into alimentary canal.

Striated at free margin in intestine where it is mainly absorptive in function.

"Goblet or chalice cells" secrete mucin.

Low columnar or cubical epithelium.

5. **Ciliated Epithelium**—Lines respiratory tract, fallopian tubes and uterus, ventricles and canals of cerebrospinal axis.

May be arranged in single layer or in several layers.

Free border provided with a series of hairlike processes termed CILIA which, while cell is alive, show constant lashing movements.

Nature and functions of ciliary movement.

Effect of narcotic agents (alcohol, ether, chloroform, etc.) on movement.

6. **Glandular Epithelium**—Found lining tubules and saccules of secreting glands, such as salivary glands, pancreas, liver. Sometimes called secretory epithelium.

Cells differ in form in different glands, but are usually cubical or polygonal.

All are characterized by presence of granules in protoplasm, which are abundant when cells are resting, and disappear when cells have been actively secreting.

7. **Sensory Epithelium**—Cells of ectodermic origin which become modified to form the receptive structures in the organs of the special senses, hearing, taste, smell.

Nerve fibers end in relation to these cells and carry impressions from them to the sensorium in the brain.

## II. CONNECTIVE TISSUES

These form mainly inactive, supporting structures, binding organs and parts of organs together.

They contain a comparatively large amount of intercellular material or ground substance in which cells lie scattered, singly or in groups.

1. **Mucoid Tissue**—Embryonic connective tissue sometimes termed Wharton's jelly.

Found in umbilical cord of fœtus and in vitreous humour of eye in adult.

2. **Connective Tissue Proper**—Several varieties—areolar tissue, tendon, ligament.

Consists of fibers (white and yellow) and several kinds of connective tissue cells.

In **areolar tissue,** which is found under the skin, the fibers are loosely arranged and are mostly of the white variety. This tissue is elastic and permits of the free movement of the skin on the parts below.

A somewhat denser variety of this tissue forms sheaths for mus-

cles, tendons and nerves, and surrounds bone (periosteum) and cartilage (perichondrium).

**Tendon** consists of dense bundles of parallel white fibers with rows of c. t. cells between. It contains few elastic fibers.

In ELASTIC TISSUE, such as the ligamentum nuchæ, or outer coat of blood-vessels, yellow fibers predominate, with fine white fibers between the bundles.

3. **Adipose Tissue**—Developed from young connective tissue by deposition of fat in c. t. cells which are then termed fat cells.

Cell in envelope swollen and rounded with nucleus squeezed to one side.

Cells are usually arranged in clusters which are vascular.

Fatty tissue found in almost every part of body but most abundant under skin, around kidneys and heart, on omentum and mesentery, and in bone marrow.

4. **Cartilage**—Three varieties. Found covering articular ends of bone (HYALINE CARTILAGE); between bodies of vertebræ as intervertebral discs (WHITE FIBRO-CARTILAGE); in epiglottis, lobe of ear, and Eustachian tube (YELLOW ELASTIC CARTILAGE).

In hyaline cartilage the cells, in groups of two or more, are surrounded by a capsule and imbedded in a hyaline (ground glass) matrix.

Other forms are more closely related to fibrous tissue.

5. **Bone**—Bone may be looked upon as a connective tissue in which the matrix or ground substance is solidified and hardened by the deposition in it of lime salts. The connective tissue cells which take on a bone forming character are termed **osteoblasts.** When they become enclosed in the layers or lamellæ of calcified material which they lay down, they are termed bone cells or **bone corpuscles,** the spaces in which they lie are termed **lacunæ** and the minute passages leading from one lacuna to another, **canaliculi.**

Bone is said to be **compact** or **spongy** according to the density of its structure. In long bones the shaft consists of compact or dense bone while the spongy variety is found at the ends. The cavity in the center of the shaft is known as the **medullary cavity** and contains the **bone marrow.**

Bone may be developed directly from membrane (e. g. the periosteum which surrounds it) or it may be preceded by cartilage. The growth in thickness is brought about by the deposition of layer after layer of compact bone underneath the periosteum, while the increase in length is due to the transformation of cartilage at the ends. At each end of a long bone there is a plate of cartilage termed the **epiphysis** and there is a continual growth of bone from these plates; when the bone reaches its full length growth stops, and the epiphyses are gradually replaced by osseous tissue. If, from any cause, the epiphyses is diseased, or damaged, or removed,

no further increase in length will take place at that end, hence the surgeon's anxiety, in operations on joints, to preserve if possible the epiphyses; if these are removed in a growing person the result is a shortened limb.

At the same time that the bone is growing thicker, by deposition on its outer surface from the periosteum, the medullary cavity is also increasing in size and this modeling is effected by **osteoclasts,** large connective tissue cells, whose function it is to absorb bone. This hollowing out prevents the bone from becoming too heavy but does not proceed so far as to unduly diminish its strength.

Although bone is hard, and apparently resistant, it is easily moulded by prolonged pressure, e. g. the growth of a tumour pressing on a bone, will cause its absorption and lead to distortion, if given sufficient time. That growing bone can be greatly modified in shape by persistent pressure is shown by the deformed feet of Chinese women due to tight bandaging in childhood.

Bone in the recent state contains about 50% of water. The solid constituents consist of **organic matter,** one part, and **inorganic matter,** two parts. The organic or animal matter is chiefly collagen which is converted into gelatin by boiling, while the inorganic matter is composed of earthy salts, mainly calcium phosphate, calcium carbonate, calcium fluoride with magnesium phosphate in small amount.

All the inorganic constituents may be removed by immersing the bone in dilute nitric or hydrochloric acid for some weeks, and the organic matter may be got rid of by burning. After either operation the bone retains its shape, but in the one case it is soft and pliable, and in the other brittle and easily crumbled.

In early life the bones contain more organic matter than in the adult and, consequently, are less rigid and not so readily fractured. As age advances, the proportion of inorganic matter increases, and the bones become more brittle. In extreme old age, the weight of the body alone may be sufficient to fracture the neck of the femur, for example.

Since bone contains a large proportion of lime salts it is essential, especially in young children where bone formation is very active, that these be present in sufficient amount in the food to satisfy the demands of the tissues. No article of diet is so rich in calcium as milk and this is the best food for the young child on that account.

## III. MUSCULAR TISSUES

There are three varieties of muscular tissue,—**striated,** striped or voluntary muscle; **non-striated,** plain or involuntary muscle; **cardiac** or heart muscle.

1. **Striated Muscle** forms the so-called flesh of the body and is found in the muscles attached to the skeleton. It is under the direct

control of the will, hence the term **"voluntary"** which is applied to it.

It consists of fibers collected into bundles, and each individual muscle is made up of large numbers of these bundles or fasciculi running more or less parallel.

**Structure of Striated Muscle Fiber**—Each fiber is cylindrical in shape and is enclosed in an envelope called the **sarcolemma** on the inner surface of which many nuclei are found. The fibers rarely exceed 1½ inches in length and are usually much shorter.

Examined under the microscope, each fiber shows transverse striations caused by alternately **dim** and **clear segments** or bands. In the middle of the clear segment a line can be made out which is believed to represent the edge of a membrane—**Krause's membrane**—, and in the middle of the dim segment another line is seen named **Hensen's line.**

In preparations hardened in formalin or alcohol each fiber can be separated longitudinally into fibrils or **sarcostyles,** and between these sarcostyles a more fluid substance is present called **sarcoplasm.** Each sarcostyle shows the same cross striation as the fiber of which it is a constituent with Krause's membrane and Hensen's line also visible.

The portion of the sarcostyle included between two adjacent Krause's membranes is called a **sarcomere;** it includes one dim segment with Hensen's line in the middle, and half the clear segment on each side. **The sarcomere is the unit of muscular structure.** The sarcostyle consists of a series of sarcomeres placed end to end; the muscle fiber is made up of a number of sarcostyles lying side by side, and enclosed in an envelope, the sarcolemma; the fibers are arranged in bundles or fasciculi which usually run parallel from end to end of the muscle, terminating in its tendons; the muscle is composed of a larger or smaller number of these fasciculi, according to it size.

**Change in Contraction**—What is believed to happen when the fiber contracts, e. g. under the influence of a nerve impulse, is that the **hyaline substance** of the clear segment is absorbed into the **sarcous substance** of the dim segment which swells up with the result that the whole fiber becomes shorter and thicker. When the exciting stimulus ceases to act the hyaline substance passes back again into the clear segment and the fiber relaxes and elongates. The same change taking place in all the fibers (or in many of them), at the same time, the whole muscle contracts or relaxes as the case may be.

The fibers are not long enough to reach from one tendinous attachment of the muscle to the other, but inside each fasciculus they cohere to each other, more or less end to end.

**Motor End Organ**—Each muscle fiber is supplied by at least one erve fiber which terminates within the sarcolemma in a "motor-nd-organ" or "end-plate."

**Muscle Spindles**—Lying amongst the muscle fibers are certain organs termed "muscle spindles" which are now believed to be the terminations of sensory nerve fibers in the muscle.

Striated muscle is a very active tissue and consequently is abundantly supplied with blood vessels.

2. **Non-striated or Involuntary Muscle** is found in the walls of the hollow viscera,—lower half of gullet, stomach, small and large intestine; in the arteries, veins and larger lymphatics; in the ureters; urinary bladder and uterus; in the ducts of certain glands; in the gall bladder; and in the intrinsic muscles of the eye.

The fibers are elongated and spindle shaped; they contain a single oval or rod-shaped nucleus near the middle and show longitudinal fibrillation, but no transverse striation. They probably do not possess a true envelope like the sarcolemma of striated muscle. The cells (each fiber is a mono-nucleated cell) vary greatly in length according to the part or organ in which they are found, but do not usually exceed the 1/600 of an inch. They are joined together by a small amount of interstitial cement substance.

Non-striped muscle receives its nerve supply from the **autonomic system.**

Its blood supply is not so abundant as in the case of striated muscle.

3. **Cardiac Muscle**—The muscle fibers of the heart differ from those of plain muscle in that they show transverse striation which, however, is neither so distinct nor so regular as in voluntary muscle. The fibers are short cylinders, joined end to end by cement substance which stains dark with silver nitrate. They have usually a single nucleus and are frequently branched at the ends. They are smaller in diameter than voluntary muscle fibers and much shorter.

Heart muscle receives its nerve supply from two sources—cerebro-spinal and autonomic—which will be considered later. It has a rich blood supply.

## IV. NERVOUS TISSUE

The nervous system consists (a) of the brain and spinal cord, together with the nerves which come off from them, the whole being termed the **cerebro-spinal nervous system** and (b), a number of ganglia connected by nerve fibers lying outside the skull cavity and spinal canal, known as the **autonomic nervous system.** The brain and spinal cord together form the **central nervous system.**

If the brain or cord be cut across with a knife, and the surface of the section examined with the naked eye, it will be seen that

certain areas have a greyish appearance while others are lighter color. These consist of **grey matter** and **white matter** respectively, the former containing nerve cells, the latter nerve fibers.

**The Neuron**—Nervous tissue is usually described as consisting of nerve cells and nerve fibers; as a matter of fact, however, EVERY NERVE FIBER IS THE PROCESS OF A NERVE CELL and the two together form the **Neuron** which is the unit of the nervous system. A NERVE CELL TOGETHER WITH ALL ITS PROCESSES IS TERMED A NEURON.

The processes which are given off by the cell or cell body are of two varieties,—**dendrites** and **axon.** Every nerve cell gives off an axon which forms the axis-cylinder, the essential conducting part, of the nerve fiber, and in addition to this many cells give origin to a number of short, branching processes termed dendrites or dendrons.

Although it is convenient to describe the nerve cell and nerve fiber separately, it should never be forgotten that the two are parts of the same anatomical unit, the neuron, and that the nervous system is made up of these units. According to the neuron doctrine, each of these units is anatomically independent. The nerve fiber of one breaks up into a number of processes termed the **terminal arborisation,** and these surround the cell body of the next neuron but do not become continuous with it. There is, however, physiological continuity, for the nerve impulse is believed to have the power of jumping across the interval. This mode of junction is termed a **synapse or synapsis.**

**The Nerve Cell or Cell Body**—Nerve cells are found in the grey matter of the brain and spinal cord; in enlargments (ganglia) on the cranial and spinal nerves; in the ganglia of the autonomic system; and in plexuses found in relation to many organs such as the heart and intestine.

They vary greatly in size, shape and structural appearance. Some (UNIPOLAR nerve cells) have only a single process—the axon; others have two processes (BIPOLAR cells), and still others (MULTIPOLAR cells) have more than two processes—one axon and several dendrites.

All nerve cells have a relatively large and conspicuous NUCLEUS, with a very distinct NUCLEOLUS and sometimes more than one. The protoplasm of the cell contains large granules which stain readily with methylene or toluidine blue; these are termed **Nissl granules.** These granules, although present in the dendrites, are absent from the axon hillock.

**Chromatolysis.**—When the cells are fatigued by excessive activity these Nissl granules gradually disappear. The term **chromatolysis** or **Nissl degeneration** is applied to these changes in the

sl bodies. A similar change is produced in the cell, in a few s, by cutting across the axon or nerve fiber.

ine fibrils—the neurofibrillæ—pass through the cell body from cess to process and run out into the axon.

The nerve cells found in ganglia are generally enclosed in a transparent membranous capsule.

**Nerve Fibers** are of two varieties, medullated and non-medullated.

**A Medullated nerve fiber** has the following structure: In the center of the fiber lies the **axis cylinder;** this is the prolongation of the axon from the nerve cell and it extends, without interruption, throughout the whole length of the fiber. It consists of a number of neuro-fibrillæ and forms the essential conducting part of the fiber.

Outside the axis cylinder lies the **medullary or myelin sheath.** It is composed of a semi-fluid, fatty substance termed myelin which stains black with osmic acid.

Next to the medullary sheath, and forming the outermost covering of the fiber, is the **neurilemma** or **grey sheath.** (The myelin is sometimes called the white sheath). This is constricted at intervals of a millimeter or less, cutting the medullary sheath into segments, and these constrictions are termed the **nodes of Ranvier.** Each **internodal segment** has a single nucleus surrounded by a small amount of protoplasm.

**Non-medullated Nerve Fiber**—The structure of the non-medullated nerve fiber is the same as that of the medullated except that the myelin sheath is absent.

The nerve fibers that come off from the brain and spinal cord are medullated; those of the autonomic system are non-medullated.

The function of the medullary sheath is not understood. It may be for the purpose of insulating the axis cylinder so as to prevent the escape of the nerve impulse, but this is not certain.

**Nerves or Nerve Trunks** are made up of bundles of nerve fibers bound together by connective tissue. These bundles vary greatly in size, and the whole is inclosed in a firm fibrous sheath called the epineurium, which contains bloodvessels and lymphatics.

**End Organs**—The nerve fibers, when they reach the tissues for which they are destined, terminate in end-organs of which there is a great variety, some motor and some sensory.

**Neuroglia**—The special form of connective tissue which binds together the nerve cells and fibers of the brain and spinal cord is termed NEUROGLIA. It consists of cells (glia cells) each with a great number of short wavy processes.

## V. BLOOD AND LYMPH

The blood and lymph may be looked upon as a tissue consisting of cells—the red and white blood corpuscles and blood plates—with the blood plasma as the intercellular substance.

The cells of this tissue (blood) retain their primitive structure to a large extent and show less differentiation from the original mother cells than those of any other tissue.

It will be studied later in detail.

Lymph is practically blood without red blood corpuscles.

# PHYSIOLOGY OF MUSCLE

## PHYSICAL PROPERTIES OF MUSCLE

**Extensibility and Elasticity**—Muscle is extensible and also elastic. The two properties do not necessarily go together; a piece of putty or dough is very extensible but scarcely at all elastic; a piece of steel or an ivory ball is not extensible but very elastic.

The extensibility of muscle differs from that of a rubber band or steel spring which obeys Hooke's law that equal increments of weight produce equal amounts of extension. IN MUSCLE EQUAL INCREMENTS OF WEIGHT DO NOT PRODUCE EQUAL AMOUNTS OF EXTENSION.

If a muscle be loaded with a weight of 10 grams, say, it will be stretched to a certain point; the next weight of 10 grams will produce less effect than the first; the third less than the second, etc. This applies to all varieties of muscle.

If the muscle is not overstretched it will return to its original length, i. e., its elastic recoil is perfect.

In the body the muscles are always in a state of **elastic tension,** i. e., they are always stretched somewhat beyond their normal length, apart altogether from muscular tonus which we shall consider later. This is seen by the fact that when a muscle is cut across with a knife, the ends retract, causing the wound to gape. That is why a deep wound involving muscle must be stitched by the surgeon to bring the faces together.

Extreme fatigue diminshes the elasticity of muscle while rise of temperature, within certain limits, increases it.

The advantages of this condition of elastic tension in muscle are, 1st, that when the muscle is stimulated there is no slack to be hauled in and so no time is lost. 2d, The shocks and jars which, would be communicated to the body, if the muscles were rigid and inextensible, are greatly reduced or prevented. It plays the same part as the springs on a wagon and adds much to the smoothness with which the movements of the skeleton are carried out. 3d, Work is economized.

## VITAL PROPERTIES OF MUSCLE

These are three in number,—EXCITABILITY, CONTRACTILITY, CONDUCTIVITY.

1. **Excitability or Irritability.** A muscle responds to stimulation by contracting, i. e. changing its shape. Muscle is not alone in this respect; all living tissues are excitable or irritable and respond

to stimulation in one way or another,—a muscle fiber by contracting, a nerve fiber by conducting an impulse, a gland cell by pouring out a secretion, etc.

The **natural stimulus** for a muscle is a nerve impulse.

Haller (1739) was the first to prove that muscle can be made to contract by artificial stimulation. The ideas prevailing before his time regarding the nature of muscular contraction were peculiar. It was believed that "animal spirits" (some kind of fluid material), generated in the brain, flowed though the connecting nerve into the muscle, forcibly causing it to swell up, and thus leading to its contraction; the muscle was believed to be passive. The truth of this doctrine was easily disproved by showing, as Haller did, that a muscle removed entirely from the body, and with its nerve completely divided, can still contract when excitied.

The **artificial stimulus** for muscle may be MECHANICAL (pinch or blow), THERMAL (application of hot wire), CHEMICAL (vapor of ammonia, etc.) or ELECTRICAL.

**Electricity** is preferred as a stimulus for both muscle and nerve, 1, because its strength can be easily regulated, and 2, if not too strong, it does not appreciably damage the living tissue.

The current may be obtained from some form of electrical battery,—**galvanic or constant current,**—or from an induction machine,—**faradic or induced current.**

The apparatus required for stimulation by galvanic electreity is as follows: 1. A **battery** in the form, for example, of a Leclanché or dry cell; 2, insulated copper wires attached to **electrodes** by which the current is led into the muscle; 3, a **key** by which the electricity is turned off or on; 4, a **switch** by which it may be used to stimulate first one tissue and then another, e. g. muscle and nerve. The current passes from the positive pole of the battery, through the circuit, back to the negative pole, and the key is used to close and open this circuit.

For experimental work the mucles of the frog are very convenient, since, in cold blooded animals, the tissues continue to live a long time after they are removed from the body.

**A Nerve-muscle preparation** consists of the GASTROCNEMIUS (calf) muscle of the frog together with the SCIATIC NERVE which supplies it. If the muscle is left in position in the leg, a straw with a flag at the end, may be attached to the toes to indicate to those at a distance when the muscles contract, or, a lever may be connected with the tendo achilles.

**Stimulation of Muscle and Nerve by Galvanic Electricity**—The following experiment will show that apparently both muscle and nerve may be stimulated by galvanic electricity. A battery is connected in circuit with a key and a switch; two pairs of wires pass from the switch, the one to the muscle and the other to the

nerve of a nerve-muscle preparation By closing and opening the key, and turning the switch to the one side or the other, the muscle and nerve may be excited at will.

It will be found, from this experiment, that with galvanic electricity, a motor nerve is stimulated when the circuit is closed (current enters nerve) and again when the circuit is opened (current leaves nerve) but not while the current is flowing through the nerve, if it does not vary in strength In the case of the muscle, however, stimulation takes place at closure, at opening, and also while the current is flowing through.

**Is muscle directly excitable?** The above experiment, nevertheless, does not prove that the muscle tissue itself is directly excitable. Why? The whole muscle is made up of a great number of muscle fibers each of which is provided with a motor end-plate, connected with a nerve fiber. Since the wires are stuck into the muscle there is no reason why these nerve fibers or end-plates should not be stimulated and so lead to an indirect response from the muscle fibers.

John Reid was the first to prove that muscle can be directly stimulated by electricity. He divided the sciatic nerve of a rabbit (when a nerve is cut off from its cell of origin it undergoes degeneration and ceases to conduct an impulse), and at the end of two or three weeks, applied electrodes to the muscles supplied by the degenerated nerve; these contracted when the current was sent through them, and this could not be the indirect result of nerve stimulation.

**Claude Bernard's Experiment**—This may also be proved by eliminating the motor end-plates by means of curara. **Curara** is a drug used by the American Indians as an arrow-poison. It has the power of producing voluntary muscular paralysis when injected under the skin. In the neuro-muscular apparatus there are four elements to be considered, the NERVE CELL in the spinal cord, the NERVE FIBER, the MOTOR END-PLATE, and the MUSCLE. Claude Bernard proved experimentally that the poison **curara acts specifically on the end-plates,** paralyzing them, so that impulses from the nerve to the muscle fibers are blocked at this point. This is a convenient way to get for experimental work, physiologically pure muscular tissue free from nerve elements.

If now we repeat the experiment on the stimulation of muscle and nerve by galvanic electricity, using a curarized muscle, we get the same effect from the muscle as before, showing that it is capable of being directly excited.

**Faradic Electricity** may also be employed to excite muscle and nerve. It is obtained by the use of some form of induction machine. (For description of induction machine consult some book on physics). Du Bois Reymond's inductorium is the form most fre-

quently employed in physiology. The PRIMARY COIL is connected with a BATTERY and a SIMPLE KEY, the SECONDARY COIL with ELECTRODES applied to the tissues, and a SHORT-CIRCUIT KEY.

When the key is closed in the primary circuit an instantaneous shock is received from the seconday coil, and when the key is opened in the primary another instantaneous sock is received from the secondary, but when the current is flowing through the primary circuit no effect is produced in the secondary, if the current does not vary in strength. The effect of the primary on the secondary is diminished by increasing the distance between the two, and vice-versa.

(Experimental demonstration to show that the break shock is stronger than the make).

Faradic electricity is the more efficient stimulus for nerve and galvanic electricity for muscle.

## RESULTS THAT FOLLOW STIMULATION OF MUSCLE

I. Chemical change.
II. Mechanical change (contraction).
III. Production of Heat.
IV. Production of Electricity.

## I CHEMICAL CHANGE IN MUSCLE FOLLOWING STIMULATION

The POTENTIAL energy of the chemical compounds in the muscle becomes transformed into the KINETIC energy of contraction (mechanical), heat, and electricity, under the influence of the stimulus.

Chemical change is always going on in muscle, even in the so-called resting state, but it is greatly increased when the muscle contracts. The main products are **carbon dioxide ($CO_2$) and sarcolactic acid.**

**Production of Sarcolactic Acid**— Resting muscle is alkaline, but if an excised muscle be made to contract for some time it becomes acid. This may be shown by the following experiment: Take two test tubes containing a solution of litmus and place a frog's gastrocnemius muscle in each. Stimulate the one muscle with interrupted shocks but not the other. The contracting muscle will soon change the layer of litmus solution in contact with it from blue to red, indicating the presence of an acid, while no such effect will be produced by the resting muscle. Analysis will show the substance produced to be sarcolactic acid.

Muscles in the living body do not become acid during contraction like excised muscle because the sarcolactic acid produced is immediately neutralized by the alkaline lymph which bathes the

muscle; the effect is a diminution in the alkalinity of the tissues but these never become acid in the living state.

**Production of $CO_2$.**—That the production of $CO_2$ is increased during contraction of muscle is shown by the following experiment:

Two tightly stoppered flasks, with an air inlet and outlet, are taken, and the hind limb of a frog suspended in each. The outlet is connected with a bottle containing a saturated solution of BARIUM HYDRATE, by rubber-tubing, and that again with a water ASPIRATOR by which a stream of air can be drawn through the two systems. (Copy diagram). One muscle is tetanised but the other is not. It will be found that the barium solution connected with the contracting muscle will become MILKY sooner than the other. This proves that $CO_2$ is produced in greater amount in the active than in the resting muscle.

Barium hydrate, $Ba(OH)_2$, which is soluble, when brought into contact with $CO_2$, is converted into barium carbonate, $BaCO_3$, which is insoluble, and water, according to the following equation:

$$Ba(OH)_2 + CO_2 = BaCO_3 + H_2O.$$

The formation of $BaCO_3$ gives the white precipitate.

Some degree of cloudiness will appear in the tube connected with the resting muscle indicating that a small amount of $CO_2$ is produced in it.

**Glycogen** is a very important constituent of muscle and this is found to diminish as contraction goes on; in exhausted muscle it may disappear altogether. The glycogen is derived from sugar, in the form of glucose, which is brought to the muscle by the blood. This glucose is transformed, by a process of dehydration, into glycogen in the muscle and the stored up glycogen is believed to be the source of the sarcolactic acid and the $CO_2$.

The changes in the protein constituents of the muscle during contraction have not been determined but they are believed to be unimportant. Some of the products of protein metabolism, together termed NITROGEN EXTRACTIVES, are probably increased during contraction; the chief of these is CREATIN.

**Respiration of Muscle**—If an excised muscle is inclosed in a bell-jar containing air of known composition, and left for half an hour, say, it will be found on removing the muscle that the air has lost oxygen and gained $CO_2$. This shows that even resting muscle, removed from the body, respires, i. e. takes in oxygen and gives off $CO_2$. If the inclosed muscle be made to contract, the amount of $CO_2$ given off will be greatly increased and also the amount of oxygen taken up.

**Alizarin Blue Experiment**—Muscle in the living body has a great affinity for oxygen, so much so, that it will remove the oxygen from chemical combination. This can be proved by the following experiment:

Inject a solution of **alizarin blue**, one of the aniline dyes, under the skin of a live frog; it will be found when the animal is killed half an hour afterwards, that the blood is tinted blue but the muscles have their normal color. On being exposed to the air, however, the muscles take on a blue tint. The explanation is that when the alizarin blue is carried to the muscles by the blood it is **deoxidized** and rendered colorless by them, while the blood has no power to do this. When the dead muscle is exposed to the air oxygen is again taken up by this colorless compound and alizarin blue reformed.

## II MECHANICAL CHANGE OR CONTRACTION OF MUSCLE

Contractility appears to be the specific property of muscle, but muscle is not the only contractile tissue in the body. This property is also possessed by cilia and by certain of the white blood corpuscles which show amœboid movement.

When a muscle contracts, each fiber, and consequently the muscle as a whole, CHANGES ITS SHAPE; it becomes shorter and thicker but it shows NO CHANGE IN VOLUME. If the gastrocnemius muscle of a frog be placed in a flask drawn out to a narrow neck, and filled to a definite mark with normal saline, and if the muscle be then made to contract by single shocks, the level of the fluid does not alter. This shows that there is no change in the volume of the muscle.

**Myographic Record of Muscular Contraction**.—For the proper study of muscular contraction the following pieces of apparatus are required: A **lever** to be attached to the muscle; a **recording surface** consisting of a revolving drum covered with smoked paper; a Du Bois Reymond **inductorium** with **battery** and **keys** for stimulation; a **tuning-fork** for recording time on the moving surface. The term **Myograph** (muscle writer) is applied to the lever, revolving drum and time writer together.

By the following method the record or graph of a simple muscular contraction may be obtained.

A frog's gastrocnemius nerve-muscle preparation is fixed to a strong support and the tendo-Achilles attached to the lever, the writing point of which is brought against the revolving drum. To the nerve is applied a pair of electrodes connected with the secondary coil of the inductorium. The drum is started rotating and by means of an automatic key, attached to the drum, in the primary circuit, a single break shock is given to the nerve from the secondary. This can be done by moving the secondary coil so far away from the primary that the make shock is eliminated. The horizontal line drawn around the drum while the muscle is at rest is called the **abscissa** or zero line.

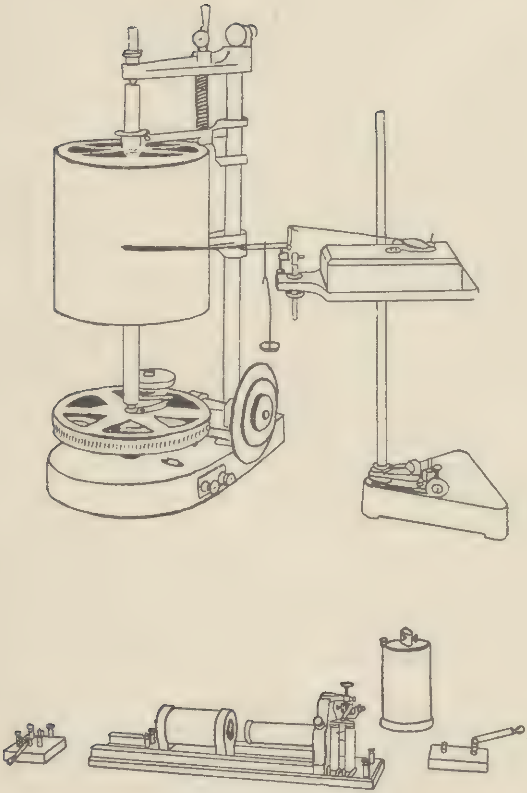


Fig. 2

When the muscle receives the stimulus it contracts and raises the lever, the graph or contraction curve or **myogram** being written off on the revolving drum. The rate at which the drum is moving is determined, at the same time, by the vibrating tuning-fork.

**Simple Muscular Curve**—On examining the record, which is usually known as a simple muscle curve, it will be found to show three phases or periods: 1, the LATENT PERIOD, 2, the CONTRACTION PERIOD, 3, the RELAXATION PERIOD.

The muscle does not respond immediately on receiving the stimulus; the time that intervenes between the application of the stimulus and the beginning of the contraction is called the **latent period.** This, in a frog's muscle, measures about 1/100 of a second, at ordinary room temperature.

If three perpendicular lines be drawn through the curve, the first at the point where the curve leaves the abscissa, the second where it reaches its maximum height, and the third where it returns to the abscissa when the muscle has relaxed again, the **contraction period** is included between the first and second of these lines and the **relaxation period** between the second and third. The contraction phase lasts about 4/100 and the relaxation phase about 5/100 of a second. The whole contraction, from the application of the stimulus to the end of relaxation, including the three phases or periods, occupies about 10/100 or 1/10 of a second.

**Influence of Various Conditions on Simple Muscle Contraction.**

(a) **Strength of Stimulus**—A SUBMINIMAL stimulus is one not sufficiently strong to bring about contraction of the muscle; a MINIMAL stimulus is one which is just able to make it contract; a MAXIMAL stimulus is one which is capable of bringing out the maximal or greatest contraction of the muscle; a SUPERMAXIMAL is any greater than a maximal, and a SUBMAXIMAL is any between minimal and maximal. It is to be kept in mind that a maximal stimulus is not the strongest that the induction coil is capable of producing, but that which will produce the greatest effect on the muscle. It is useless and inadvisable to employ a supermaximal stimulus because it may damage the tissue.

This gradation of effect following progressive increase in strength of stimulus is shown by striated and plain muscle, but not by heart muscle, as we shall see later. Later investigation, however, would appear to show that each muscle fiber, whether in striated, plain or cardiac, muscle gives the all—or nothing response when stimulated.

With stimuli between minimal and maximal, the stronger the stimulus, the shorter is the latent period and the higher is the curve of contraction.

(b) **Resistance to be Overcome,** i. e. **Load**—The heavier the load the longer is the latent period and the whole duration of the

curve, and the shorter is the height of contraction. In this case the increase in the length of the curve is mainly due to the prolongation of the relaxation phase. The effect of the extensibility of the muscle is to increase the latent period, but apart from this, the true, corrected latent period is lengthened.

(c) **The internal condition of the muscle itself influences its contraction. Fatigue**—As fatigue sets in the LATENT PERIOD and the WHOLE DURATION of the contraction INCREASES, while the HEIGHT DIMINISHES, the chief effect again being on the period of relaxation.

**"Treppe"**—When a muscle is excited by a series of stimuli of equal strength, at intervals of one second, say, the first few contractions become progressively higher and higher until a maximum is reached, and then fatigue begins to manifest itself. This is called **"treppe"** or the **"stair-case" phenomenon** because the curves obtained on a slowly revolving drum resemble somewhat the steps of a stair.

The cause of this treppe is believed to be the development of $CO_2$ within the muscle, whereby its irritability is increased at first, and then diminished. The same result is obtained from all three varieties of muscle, and from nerve. It indicates that the effect of the activity of the tissue is, in the beginning, beneficial to the tissue because it increases its irritability.

**Cause of Fatigue in Muscle**—The fatigue of muscle is mainly due to the accumulation of the products of contraction—sarcolactic acid and $CO_2$. This is proved by the following experiments:

1. If the extract of fatigued muscle is injected into a fresh animal, this animal on being made to exercise, rapidly shows signs of fatigue.
2. If the blood of a fatigued dog be injected into a fresh one, fatigue quickly appears in the latter. This proves that the fatigue products pass from the muscle into the blood of the general circulation.
3. Fatigue can be rapidly induced in a muscle by feeding it with a weak solution of lactic acid.
4. An isolated muscle is much more easily exhausted than one through which the blood is circulating. In the one case the poisonous products are allowed to accumulate in the muscle, in the other case they are washed away by the blood and lymph.

It is a well known fact that massage helps to restore fatigued muscles; by this treatment the fatigue products are squeezed out into the circulation.

To a certain extent fatigue is due to the using up of the stored material within the muscle whose breaking down results in the contraction, but this is a less important factor than the other.

**Seat of Fatigue in Muscle**—The question that next arises is,

when a muscle is stimulated through its nerve, what is the seat of fatigue—the nerve fiber, the muscle fiber, or the motor end-plate? Since it will be seen later that a nerve fiber cannot be fatigued, it must be either the muscle or the end-plate, and there is reason to believe that it first appears in the end-plate. The following experiment seems to prove this:

Arrange apparatus to stimulate a muscle through its nerve, once every half second, until it is completely fatigued and unable to raise the lever with the weight attached; then throw the stimulus, by means of a switch, directly into the muscle; it will begin to contract again.

**Mosso's Ergograph**—The onset and effects of fatigue in human muscle have been studied by Mosso with an instrument, devised by him for the purpose, termed the **ergograph.** A weight of say 10 pounds is lifted, by a sudden voluntary flexion of the middle finger to which it is attached, once a second, to the beat of a metronome. A writing point moving on the surface of a slowly revolving drum records, as an ordinate, the height to which the weight is lifted each time. A small belt is attached to the mid-finger which lifts the weight, the other fingers being strapped down to prevent them from assisting, thus one set of muscles alone (the flexors of the middle finger) is brought into play. The graphs recorded show the rapidity with which fatigue sets in.

Using this instrument, the following points, among others, were made out by Mosso:

"1. If sufficient time is allowed between contractions little or no sign of fatigue is apparent. With a load of 6 kilograms (about 14 pounds), for instance, the flexor muscles of the finger showed no fatigue when a rest of 10 seconds was given between contractions.

2. After complete fatigue, with a given load, a very long interval (2 hours) is necessary for the muscle to make a complete recovery and give a second record as extensive as the first.

3. After complete fatigue efforts to still further contract the muscle greatly prolongs this period of complete recovery—a fact that demonstrates the injurious effect of straining a fatigued muscle.

4. The power of a muscle to do work is diminished by conditions that depress the general nutritive state of the body or the local nutrition of the muscle used; for instance, by loss of sleep, hunger, mental activity, anæmia of the muscle, etc.

5. On the contrary, improved circulation in the muscle—produced by massage, for example—increases the power to do work. Food also has the same effect, and some particularly interesting experiments show that sugar, as a soluble and easily absorbed foodstuff, quickly increases the amount of muscular work that can be performed.

6. The total amount of work that can be obtained from a muscle is greater with small than with large loads, since fatigue sets in more rapidly with the larger loads.

7. Marked activity in one set of muscles—the use of the leg muscles in long walks for instance—will diminish the amount of work obtainable from other muscles such as those of the arm.

It is very evident that the instrument may be used to advantage in the investigation of many problems connected with gymnastics, dietetics, stimulants, medicines, etc." HOWELL.

**Sensation of Fatigue**—The feeling of discomfort which is experienced in fatigued muscle probably results from stimulation of the sensory nerve terminations (muscle spindles) within the muscle and tendon. This acts as a safeguard against excessive muscular activity and overstrain.

(d) **The Temperature of Muscle affects the Character of its Contraction**—The application of **cold** to a muscle has an effect similar to that of fatigue—the latent period is increased, the height of the curve diminished, and the duration of the whole curve lengthened, mainly by a prolongation of the relaxation phase. **Heat,** up to a certain limit, has the opposite effect,—the latent period is shortened, the height is increased and the length of the whole curve shortened.

At a temperature of about 37° C. for the frog, the muscle loses its irritability and dies. At a certain temperature, known as the **optimum temperature,** which differs for different animals, muscle transforms energy most rapidly and most economically.

(e) **Drugs**—Certain drugs have a pronounced effect on the character of the simple muscle curve. The best example is the alkaloid **veratrin.** Under the influence of this drug the contraction is very greatly prolonged, the effect again being on the relaxation phase.

### Compound Muscular Contraction or Tetanus

So far we have considered the contraction of a muscle following a single stimulus; when a muscle receives a series of stimuli in rapid succession, there being no time to relax from one stimulus before the next one enters, it gives no longer a simple twitch but a compound contraction or tetanus.

If the rate of stimulation is so rapid that the muscle shows no external sign of relaxation between stimuli, the record of this compound contraction on a revolving drum will be a continuous line; this is known as **complete tetanus.** When, however, the rate of stimulation is not sufficiently rapid, the muscle will relax more or less after each stimulus, and the record will show a wavy line, each secondary curve representing a muscular contraction; this is known as **incomplete tetanus.**

The rate of stimulation necessary to produce complete tetanus will vary with the kind of muscle used and with its condition, (whether fatigued or not, etc.) and temperature. For insect's muscle it will require 300 stimuli per second, for fresh frog's muscle, at room temperature, about 25 per second and for non-striped muscle one stimulus applied every five seconds may be sufficient; it will depend on the rapidity of relaxation shown by the muscles in simple contractions.

There is evidence, however, to show that the rate of compound muscular contractions can be more rapid than that necessary to produce complete tetanus (See Muscle Sound.)

**Voluntary muscular contractions** are tetanic in character; not even the most rapidly executed voluntary movement is a simple muscle twitch.

## Muscular Work

Work (W) is defined as the product of the load (l) into the height (h) to which it is lifted.

$$W = l \times h.$$

When a muscle contracts without lifting a load no work is done, for $W = o \times h = o$. Again, when a muscle contracts but is unable to raise the load attached to it no work is done, for $W = l \times o = o$.

The English unit of work is the **foot-pound**; the height is measured in feet and the weight in pounds. The French unit is the **gramme-metre** or **gramme-millimeter**, the height being measured in metres or millimeters and the load in grammes.

**The amount of work performed by a frog's muscle** may be estimated by loading it with known weights and measuring the height of the contractions recorded as ordinates on a stationary drum moved by hand. The lengths of the ordinates must be reduced for lever-magnification, and then the reduced height in millimeters multiplied by the load in grammes.

If such an experiment be performed it will be found that the work done by a muscle increases with the load until the muscle is overloaded. There is one load for each muscle in lifting which it will do more work than with either a lighter or a heavier load, and this is called the **optimum load**, i. e. the load in lifting which the muscle can do most work.

**The absolute power of a muscle** is the load which the muscle is just unable to lift. This depends on the cross-section of the muscle and on its energizing power.

The height to which a muscle can lift a weight depends on the length of the muscle, the weight to be lifted, and the quality of the muscle, the stimulus always being maximal.

To get the most out of a muscle it must be excited with a **maximal stimulus,** at the **optimum temperature,** and weighted with the **optimum load.**

Insects have the most powerful muscles, weight for weight. The absolute power of human muscle is more than twice as great as that of frog's muscle per unit of the cross sectional area, and that of insect muscle is much greater still.

The power of human muscle is measured by some form of **dynamometer** adapted to the particular group of muscle to be tested. The hand dynamometer shown is used for estimating the force of contraction of the flexor muscles of the fingers.

## III PRODUCTION OF HEAT IN MUSCLE

Some heat is always being produced in muscle but the amount is greatly increased when the muscle contracts. More than eight-tenths of the total heat of the body is produced in muscle.

**Unit of Heat**—Just as in measuring mechanical energy we require a unit of work, so in dealing with heat energy we must have a unit of heat. This is termed the **calorie;** it is defined as the amount of heat necessary to raise one gram of distilled water from 0° C. to 1° C. (small calorie) or one kilogram from 0° C. to 1° C. (large calorie).

The **quantity of heat** produced by a muscle, in a definite time, may be calculated by multiplying the increase in temperature by the mass (weight) of the muscle by the specific heat of the muscle which may be taken as 0.8. For example, if a frog's muscle weighing 10 grams had a temperature of 15° C. in the resting state, and 15.1° C. after a period of contraction, then the amount of heat produced by the muscle during this period, assuming that none has been lost, will be $0.1 \times 10 \times 0.8 = 0.8$ calorie; that is the amount of heat necessary to raise eight-tenths gram of distilled water from 0° C. to 1° C.

In the case of large animals, such as the cat or dog, if the bulb of a mercurial thermometer be pushed into the muscles of the thigh (animal anæsthetised) and then the sciatic nerve stimulated, the temperature of the muscle may be raised two or three degrees in a short time. For the detection of slight rises in temperature, such as occur in the small muscles of a frog, a mercurial thermometer is not sufficiently sensitive; the thermo-electric method must be used.

**Thermopile**—Given two junctons of bismuth and antimony (or iron and German silver), if one is hotter than the other, electricity is developed in the heated junction and passes as a current through a galvanometer in circuit. From the amount of deflection of the galvanometer needle the difference in temperature between the

two junctions can be calculated. This is a **thermopile.** By increasing the number of junctions connected in series the instrument is made more sensitive.

**To determine slight changes of temperature in frog's muscle** the thermopile is used as follows: Two nerve-muscle preparations are made and one is applied to each junction (or set of junctions). One muscle is stimulated, through its nerve, to contract while the other is allowed to rest. In the contracting muscle heat is developed which generates electricity and the rise in temperature can be calculated from the amount of deflection of the galvanometer needle.

A single contraction will raise the temperature of a frog's gastrocnemius about 1/1000 of a degree centigrade.

By causing a muscle to lift a weight and at the same time measuring the heat produced in it, THE RATIO OF MECHANICAL WORK TO HEAT PRODUCTION CAN BE OBTAINED. While the best mechanical engine (gas engine) will not transform more than 25% of the total energy of its fuel into mechanical work, the other 75% being wasted as heat, a muscle (human) it has been stated will give 40% as mechanical work and the remaining 60% as heat is not wasted for it serves to maintain the temperature of the body.

## IV. PRODUCTION OF ELECTRICITY IN MUSCLE

**Galvani's Experiment**—Galvani, the professor of physiology in the University of Bologna, is credited with the discovery of animal electricity. One day when watching some frogs' legs, suspended by copper hooks, on an iron railing he observed that whenever the wind brought the muscles in contact with one of the rails they twitched. He explained the twitching, under these conditions, by supposing that the electricity is present in the tissue and that it excites the muscle when the circuit is completed.

Volta, professor of physics at Pavia, maintained, however, that the source of the electricity was the junction of the two dissimilar metals, copper and iron. The controversy lasted several years and it was finally shown that both were right, in part.

**Electric Fishes**—Long before the discovery of Galvani it was known that certain fishes had electrical properties; these were the **Torpedo** or electric ray, found in the Mediterranean, the **Malapterurus electricus,** in the Nile, and the **Gymnotus** or electric eel in South America.

These fishes are provided with a series of plates arranged parallel to each other like the elements of a galvanic battery. Each plate is supplied by a nerve from the brain through which impulses may be sent voluntarily to discharge the organ. In all electric fishes the discharges are interrupted; an active fish may give as many as 200 shocks per second; this is comparable with the compound

contractions of a muscle. This power is used by the fish to stun or kill its prey or enemies.

In the gymnotus and the torpedo these organs are modified muscles, while in malapterurus they are said to be transformed skin glands.

**The requirements for the study of the electrical changes in muscle are**—1, a senstitive GALVANOMETER or ELECTROMETER; 2. NON-POLARIZABLE ELECTRODES; 3. a BATTERY and INDUCTION COIL for stimulating the muscle.

If a frog's gastrocnemius muscle be dissected out and one end injured, as by cutting it across, and then if one electrode be applied to the cut end of the muscle and the other to the longitudinal surface, a current of electricity will pass through the galvanometer from the longitudinal surface to the cut end; this is called the **current of injury,** or the **demarcation current.** The longitudinal surface is positive, corresponding to the positive pole of an ordinary galvanic battery, and the cut end is negative.

Contrary to the opinion held by Galvani, it is now known that no current is produced by an uninjured and resting muscle. If the electrodes be applied to two points on the longitudinal surface of an uninjured muscle no effect is seen on the galvanometer, since all points on the surface are at the same potential, or iso-electric; if, however, the muscle be made to contract by stimulation at one end then a current is produced in the muscle. As the contraction wave sweeps along, the active (contracting) part of the muscle is negative to the inactive parts which are positive,—an area of depressed potential accompanies the wave of contraction. This is known as the **current of action** or the **negative variation.**

This action current is frequently taken as a measure of the activity of the muscle instead of the record produced by a lever writing on a drum, from its mechanical contraction.

**Rheoscopic Frog**—The action current of one muscle may be used to stimulate the nerve of another nerve-muscle preparation and so to cause contraction of the second muscle (see diagram). Two such preparations are known as the RHEOSCOPIC FROG.

A very striking experiment may be performed by laying the nerve of a nerve-muscle preparation, longitudinally, on the beating heart of a frog; the action current of the heart will stimulate the nerve and so the muscle will contract synchronously with the heart.

When muscle contracts tetanically it gives rise to a musical sound which can be heard by applying a stethoscope to the muscle, or demonstrated with the microphone. The note that is heard corresponds, in pitch, to the number of stimuli sent into the muscle, up to a certain point. In the case of frog's muscle when the stimulation is at the rate of 200 per second, or less, the musical note

produced corresponds, but if the rate be increased over 200 then the tone fails to rise in pitch. For mammalian muscle the limit is about 1000 per second. This shows that, even in apparently COMPLETE TETANUS, the character of the contraction is NOT CONTINUOUS but interrupted, due to what may be supposed to be a series of explosive changes in the muscle. The failure to produce tones above a certain pitch may be due to the fact that the substance exploded requires time to be re-built up, in order to be decomposed again, and if this is less than 1/1000 second in mammalian muscle, or 1/200 second in frog's muscle, then a certain number of stimuli must be ineffective. This fraction of a second is known as the **Refractory Period.**

This interrupted character of muscular contraction, with high rates of stimulation, can also be proved by the fact that each stimulus is followed by a current of action in the muscle which can be demonstrated with the string galvanometer, up to certain limits.

## MUSCLE TONUS

The skeletal muscles are always in a state of semi-contraction so long as their nervous connection with the spinal cord or brain is complete; this is known as MUSCLE TONUS.

**Cause of Muscle Tonus**—It was at one time believed to be due to the automatic discharge of a succession of feeble impulses being showered down on the muscle, through its motor nerve, from the spinal cord, since, if this nerve is divided, the tonus disappears. The same thing happens, however, that is, loss of tonus, if the afferent nerve root entering that segment of the cord from which the motor root arises, be divided; therefore this is a reflex phenomenon.

A living muscle, therefore, with its nerve connections intact, is never in a condition of rest, although not in visible contraction; it is always the seat of chemical change and of heat production even in the so-called resting condition.

## CONDUCTIVITY OF MUSCLE

This is the last of the three vital properties of muscle (irritability, contractility, conductivity) to be considered. Muscular tissue has a certain power of transmitting disturbances, produced in it at any point, through its substance, although this is the specific property of nerve fibers.

If a curarised muscle (why curarised?) be stimulated at one end, the **wave of contraction** initiated there will pass to the other end, the disturbance being conducted from fiber to fiber.

**Method of Measuring Rate of Muscular Contraction Wave**—A frog's curarised muscle (preferably one with parallel fibers such as the sartorius) is pinned out on a cork plate and two light levers laid across it, about an inch apart, their writing points being brought against a rapidly revolving drum and on the same vertical line. The muscle is stimulated at one end by a single induction shock, and the contraction wave, which starts at that end, sweeps along the muscle raising first the proximal lever and then the distal. Two curves will be written off on the drum, the one beginning before the other. A tuning fork tracing is taken underneath and the time interval between the beginnings of the two curves observed. The distance on the muscle between the two levers is then measured. This will give all the data necessary for calculating the rate in feet or meters per second.

For example, suppose the time interval between the beginnings of the two curves to be 1/120 second (i. e. the time taken for the wave to pass from the proximal to the distal lever), and the distance between the two levers one inch; then the wave in one second would travel 120 inches or 10 feet.

The rate in frog's muscle is found to be about 10 feet per second; in human muscle about 30 feet per second.

## RIGOR MORTIS

Muscle when dead loses its irritability, becomes stiff and rigid and passes into a condition known as **rigor mortis** or **death stiffening.** The cause of this is believed to be the coagulation of the protein constituents (or some of them) of the muscle. In some respects it resembles the clotting of blood.

A somewhat similar condition is brought about by exposing the muscles to too high a temperature; this is known as **rigor caloris** or **heat stiffening.** Sarcolactic acid is developed in the process in both cases.

In the human subject rigor mortis appears first in the muscles of the jaw; then in the neck, arms and trunk, in that order, and lastly in the muscles of the leg. It passes off in the same order.

The time of onset varies greatly; it usually supervenes from one to seven hours after death, but it may come on a few minutes after or it may be delayed for many hours, depending no the condition of the muscle. Its appearance is HASTENED BY EXHAUSTION due to starvation, fatigue or wasting disease. Rigor usually lasts from 24 to 36 hours but it may continue for as long as six days; if it comes on quickly it passes off quickly. The disappearance of rigor seems to be due to the softening of the coagulated proteins, by the action of autolytic ferments, in the presence of sarcolactic acid.

## ACTION OF MUSCLES ASSOCIATED WITH THE SKELETON

The skeleton gives support and protection to the soft parts of the body and is clothed mainly by muscles whose action is under the control of the will, hence they are called **skeletal** or **voluntary** muscles. They are concerned with the movement of one part in relation to another, and also with the locomotion of the body as a whole.

The muscles associated with the limbs cause the movement of bones at joints, and according to the nature of these movements, the limb muscles are grouped as **flexors, extensors, abductors, adductors,** and in the forearm, **supinators** and **pronators.**

In addition to the limb mucsles other groups are the **neck muscles** which move the head on the trunk; muscles related to other regions of the **spinal column**; muscles forming the **walls of the thorax** (external and internal intercostals) and **abdomen**; the **diaphragm,** separating the thoracic and abdominal cavities; the **facial muscles** or muscles of expression; muscles of the **tongue**; muscles of the **eyeball**; and lastly the **dermic or skin muscles,** rudimentary in man, but well developed in certain of the lower animals, e. g the horse.

Each muscle is a separate organ, surrounded by a capsule of connective tissue (the deep fascia) which separates it from its neighbors.

In describing a muscle anatomically the following points must be stated—its ORIGIN, COURSE and INSERTION; its RELATIONS to neighboring structures, and its NERVE SUPPLY.

The great majority of voluntary muscles are inserted into bones, and when they contract, movement of the bones takes place at joints, and the action of the muscle will depend on the relation between, 1, the point of insertion; 2, the point of application of the resistance to be overcome; and, 3, the joint or fulcrum around which the movement takes place.

Examples of each of the **three orders of lever** are to be found in the body.

**First Order**—Power (insertion of muscle) at one end, weight or resistance at other end, and fulcrum (joint) between. Example—action of triceps muscle in extending the forearm.

**Second Order**—Power at one end, fulcrum at the other end, and the weight or resistance between. Example—action of the muscles attached to the lower jaw that open the mouth.

**Third Order**—Weight or resistance at one end, fulcrum at other, and application of power between. Example—action of biceps muscle in flexing the forearm at the elbow joint.

It must be remembered that even the simplest movement, such as bending the finger, for example, requires the **co-ordinated action of several muscles.** This is effected by **nerve centers** situated in the brain and spinal cord.

## NON-STRIATED, PLAIN OR INVOLUNTARY MUSCLE

The physiological properties of plain muscle differ from those of striated mainly in three respects: 1, its nerve supply comes from the AUTONOMIC SYSTEM so that it is not under the control of the will like striped muscle; 2, it is MORE SLUGGISH in its response to stimulation than striped muscle; and 3, it appears to have the power of contracting RHYTHMICALLY, without nervous stimulation, which striated muscle has not.

The contraction of plain muscle is so sluggish, in all its phases, that a single contraction may last for minutes instead of the fraction of a second as in striated muscle; the latent period may be more than half a second.

The various forms of artificial stimulation used in the case of striped muscle are effective for plain, but, as a rule, the latter requires a much stronger stimulus.

**Rhythmicity**—If a strip of non-striated muscle—e. g. from the frog's stomach—be attached to a lever the point of which is brought against a slowly revolving drum, the muscle being immersed in Ringer's solution to keep it alive, a WAVY CURVE will be obtained due to the slow and irregular contractions and relaxations of the muscle. If a striated muscle is similarly treated the curve obtained will be a straight line unless the muscle be stimulated directly or through its nerve. A good example of this rhythmical property of plain muscle is to be found in the peristaltic movements of the intestine by which its contents are driven onwards.

**Heart Muscle**—The physiological properties of heart muscle will be more profitably considered under the circulation.

## PHYSIOLOGY OF NERVE

Coming off from the brain and spinal cord, which together form the central nervous system, are 43 pairs of nerves—12 pairs from the brain (**cranial nerves**) and 31 pairs from the cord (**spinal nerves**). Each of the spinal nerves arises from the side of the spinal cord by **two roots**—the anterior or ventral root, and the posterior or dorsal root, the latter being characterized by a swelling or ganglion—the posterior root ganglion. A short distance from their origin both roots unite to form the spinal nerve.

**The autonomic nervous system** lies OUTSIDE THE CENTRAL NERVOUS SYSTEM but is connected with it; this gives nerve fibers to non-striped muscle and various other tissues.

**Anatomical Classification of Nerve Fibers**—Nerve fibers (or any tissue) may be classified anatomically or physiologically. Anatomically they are of two kinds—MEDULLATED fibers and NON-MEDULLATED fibers, the structure of which has already been described.

**Physiological Classification of Nerve Fibers**—Classified physiologically, that is, according to their function, nerve fibers may be divided into two main groups—**efferent** (out-going) fibers carrying impulses away from the central nervous system, and **afferent** (incoming) fibers carrying impulses towards the central nervous system. Each of these groups may be further subdivided.

**Efferent fibers are subdivided as follows:**

1. MOTOR
   - Motor to voluntary muscles.
   - Vaso-motor,—to bloodvessels.
   - Cardio-motor,—to heart.
   - Viscero-motor,—to viscera such as stomach, intestine, etc.
   - Pilo-motor,—to hair muscles.
2. SECRETORY
   - To salivary glands.
   - To stomach.
   - To pancreas, etc.
   - To sweat glands.
3. INHIBITORY
   - For each variety of motor fiber.
   - For each variety of secretory fiber.

**Afferent fibers are subdivided into:**

1. Those fibers that carry impulses into the central nervous system which **affect consciousness** (**sensory**).

2. Those fibers that carry impulses into the central nervous system which **do not affect consciousness** (**reflex**).

**Motor Nerves**—Many nerve fibers carry impulses to muscles producing movement; these are termed motor fibers and they are subdivided according to the variety of muscle which they supply,—the skeletal muscles (motor fibers); muscular tissue of the blood-vessels (vaso-motor fibers), of the heart (cardio-motor fibers), of the abdominal viscera (viscero-motor fibers); and the erector pili muscles of the hairs (pilo-motor fibers).

**Secretory Nerves**—Another subdivision of the efferent group carry impulses to secreting glands, such as the salivary glands, causing them to pour out fluids or secretions. These are termed secretory nerve fibers, and they are subdivided according to the variety of gland tissue which they supply.

**Inhibitory Nerves**—Finally, a large number of nerve fibers are not excitatory but inhibitory, that is, impulses coming through these nerve fibers check or inhibit some action which was already taking place, it may be the contraction of a muscle, or the secretion of a gland; these are termed the inhibitory nerve fibers.

Similarly the afferent group may be subdivided into two classes according as the impulses which they convey reach the cerebrum (highest division of brain) and so affect consciousness (sensory division), or go no farther than the spinal cord and lower regions of the brain and bring about reflex action of some kind (reflex division).

When a nerve is cut across the end of the divided nerve next to the central nervous system is called the CENTRAL END and that next to the surface of the body or periphery is called the PERIPHERAL END.

**Methods of Determining Functions of Nerves**—If we wish to find out the function of a particular nerve two general methods may be employed: 1, we may **divide** the nerve and note what happens; 2, we may **stimulate** either the central or the peripheral end and note what happens. For example, if, after cutting a nerve across, we find that a certain muscle or group of muscles is paralyzed we know that the nerve is motor in function. This will be made more certain still if the muscle or muscles contract on stimulating the peripheral end of the nerve.

**Bell-Magendie Law**—It was at one time believed that all nerve fibers convey impulses or messages in both directions just like a telegraph wire, but in 1811 Sir Charles Bell proved experimentally that the **anterior roots** of the spinal nerves are **motor** in function while the posterior roots are not. He observed, in a recently killed animal, that when an anterior root was touched or pinched with forceps, certain muscles were thrown into contraction, while this did not happen when the posterior roots were excited. Later (1822) Magendie showed that in a living animal, when the **posterior**

roots were stimulated, there was evidence of **pain.** Combining the results of both experiments it was stated that the anterior roots of the spinal nerves are purely motor, the posterior roots purely sensory, and this is known as the **Bell-Magendie law.**

Since the time of Bell and Magendie it has been found that in addition to purely motor fibers many others,—vaso-motor, secretory, inhibitory, etc.—emerge in the anterior roots, and that in the posterior roots there are fibers stimulation of which causes only reflex action, so that now the more general statement may be made that ALL EFFERENT FIBERS LEAVE THE SPINAL CORD BY THE ANTERIOR ROOTS AND ALL AFFERENT FIBERS ENTER BY THE POSTERIOR ROOTS.

## REFLEX ACTION

Any action which is not directly voluntary is said to be reflex; the individual may or may not be conscious of it. For example, if the sole of the foot be tickled the leg is involuntarily withdrawn by the contraction of its muscles; this is a **reflex act,** and the subject is quite conscious both of the movement and of the sensation, but it is not voluntary. During sleep, when consciousness is in abeyance, this reflex can be elicited even more readily than in the waking state.

**Reflex Arc**—The anatomical basis of reflex action is the reflex arc. This consists of (a) an **end-organ** (the receptor) and **afferent nerve fiber;** (b) a **nerve center;** (c) an **efferent fiber** ending in a **muscle, gland cell, etc. (the effector).**

The simplest reflex arc contains two neurons—an afferent and an efferent—the synapse being situated within the central nervous system (brain or spinal cord). In more complex arcs one or more neurons may be interposed between the afferent and efferent. INTERRUPTION OF THE ARC AT ANY POINT WILL ABOLISH THE REFLEX.

**Inhibition of Reflexes**—Reflex actions (motor, secretory, etc.) may be inhibited, to a certain extent, voluntarily, or by excitation of some other receptive surface, e. g. the reflex movement called forth by tickling the sole of the foot may be prevented by a powerful voluntary effort.

**Spinal Reflexes in Decerebrate Animals**—Spinal reflexes are more easily induced in "decerebrate" (deprived of the cerebrum) than in normal animals, the reason assigned being that with the brain intact inhibitory impulses are being constantly showered down on the lower spinal centers, keeping the reflexes in check; when the cerebrum is taken away this controlling or inhibitive

influence is removed. This also explains why it is that the spinal reflexes are more easily elicited in animals low in the scale (frog) than in those higher (cat, dog, man).

**Importance of Reflexes in Medicine**—In the human subject the character of the spinal reflexes, particularly the plantar reflex and the knee-jerk, is of great value to the physician in the practice of medicine as diagnostic signs in diseases of the nervous system. The **Knee-jerk** is elicited by giving a sharp blow with the edge of the open hand to the patellar tendon in front of the knee, when the foot is suddenly and involuntarily jerked or kicked forward. This is present in all normal individuals but in the disease known as LOCOMOTOR ATAXIA it is absent. The lesion in this disease lies in the posterior nerve roots, the afferent factor in the reflex arc thus being broken. In INFANTILE PARALYSIS (poliomyelitis anterior acuta) the part primarily affected is the grey matter of the spinal cord (anterior horn). Here again the knee-jerk is absent, the arc being interrupted centrally. On the other hand, in some conditions, such as SPASTIC PARALYSIS, the knee-jerk is exaggerated. In this disease the inhibitory influences of the higher brain centers is cut off, and all the spinal reflexes are more easily called forth, just as they are in a decerebrate animal.

**Classification of Reflex Movements**—Reflex movements may be SIMPLE, CO-ORDINATED, or CONVULSIVE.

1. **Simple Reflex**—By a simple reflex is meant one in which a single muscle is affected. The best example is the WINKING REFLEX, where the single muscle of the eyelid (orbicularis palpebrarum) contracts reflexly as the result of a stimulus received from the sensitive conjunctiva.

2. **A Co-ordinated Reflex** is one in which a group of muscles are called into play so as to bring about a co-ordinated and apparently purposeful movement. This is well seen in a frog, from which the brain has been removed, so as to make voluntary movements impossible. If such a frog be suspended from a stand and a small square of blotting paper, soaked in acetic acid, be applied to the skin of the back at one side of the middle line, the limb of that side will be drawn up, and the toes directed to the spot which is being irritated by the acid so as to remove the blotting paper. Here the movement is unconscious and involuntary, nevertheless, many muscles are used in perfect co-ordination so as to bring about a series of movements with an apparently definite end.

3. **Convulsive Reflexes** are those in which a great number of muscles (possibly every muscle in the body) are brought into action, without any co-ordination, disorderly, purposeless movements being produced.

A co-ordinated reflex may be transformed into a convulsive one, 1, by strong or persistent sensory stimulation, and 2, by diminishing the resistance at the synapses in the reflex arcs.

1. When the skin of the sole of the foot is tickled, momentarily, the foot is withdrawn by the co-ordinated action of the muscles of the leg, but if the tickling be persisted in many other muscles are brought into play, not associated with the withdrawal of the foot at all, notably the respiratory and facial muscles used in the act of laughing.

2. If a small amount of **strychnine** be injected under the skin of a decapitated frog it will soon be absorbed and carried to all the tissues including the spinal cord. In such an animal the slightest stimulus applied to the skin will cause, not a simple or co-ordinated reflex, but powerful convulsive movements of all the muscles in the body. The reason given for this action of strychnine is that it diminishes the resistance, at the synapses in the reflex arcs, to the passage of the impulses that bring about contraction of the muscles.

## PROPERTIES OF NERVE FIBERS

Nerve fibers have two properties: 1, **Irritability;** 2, **Conductivity.** Like all living nerve tissues fibers are irritable, i. e. they respond to stimulation, but their specific property is conductivity.

**The natural stimulus** for a nerve fiber is some change (possibly chemical) in its cell of origin, or in its termination in a sensory surface. As in the case of muscle, **artificial stimulation** may be mechanical, chemical, thermal or electrical, and the last is preferred for the reasons given under muscle, viz.– that its strength is easily regulated, and that it does not appreciably injure the tissue.

When stimulated, naturally or artificially, a nerve impulse is initiated at the point excited and travels or is **conducted** along the fiber. No contraction or visible change of shape follows, as we saw in the case of muscle; the only known sign of the passage of a nerve impulse is an ELECTRICAL CHANGE which passes along the fiber accompanying the impulse and which is known as the **current of action.**

**The electrical changes in nerve** are studied in the same way and with the same apparatus as in muscle. A divided nerve will give a **current of injury** and an active nerve (engaged in conducting a nerve impulse) a **current of action** just as we saw in muscle, and this current of action is taken as the OBJECTIVE SIGN OR INDEX OF FUNCTIONAL ACTIVITY in investigating the physiological properties of nerve fibers. A dead nerve will not conduct an impulse and shows no action current.

**Irritability of Nerve Fiber**—The response of a nerve to any stimulus depends on three factors—(a) the degree of excitability of the nerve; (b) the strength of the stimulus; and (c) the duration of the stimulus.

**Summation of Stimuli**—The duration of a stimulus, as well as its strength, is important. A subminimal stimulus continued for some time will ultimately produce an effect. This is known as the **summation of stimuli.** If a decerebrate frog be suspended from a stand and the toes of one hind limb dipped into dilute sulphuric acid, 1 in 50, the limb will be almost IMMEDIATELY withdrawn reflexly; if, however, the irritating acid be more dilute, say 1 in 500, then it may be MANY SECONDS before the limb is withdrawn. In the latter case the stimuli are too feeble individually to produce any result but may do so when they are summated or added together.

## Conductivity of Nerve Fiber

By this is meant the capacity of a nerve fiber to conduct an impulse initiated at any point on its course by natural or artificial stimulation. This is the specific property of nerve fiber just as contractility is the specific property of muscle fiber.

**Rate of Nerve Impulse**—The velocity with which an impulse sweeps along a nerve fiber was first successfully measured by Helmholtz. He stimulated the sciatic nerve of a frog's nerve-muscle preparation first at a point near the muscle, (a), and then at a point near the spinal cord, (b), i. e. far away from the muscle, and measured the time interval between the beginnings of the two curves recorded on a revolving drum. Knowing this interval in fractions of a second, and the distance between the two points (a) and (b) on the nerve, the rate in feet or meters per second can be calculated. For example, suppose the two points on the nerve are two inches apart and that the second curve begins 1/550 second later than the first, then the distance travelled in one second will be $2 \times 550 = 1100$ inches or $91\frac{2}{3}$ feet per second.

The velocity in the frog's motor nerve, at room temperature, Helmholtz found to be about 90 feet per second. In human nerve it is somewhat greater, viz.: about 110 feet per second.

Both the velocity and the strength of the impulse are modified by temperature, by narcotic drugs, and by mechanical pressure.

In **cooled nerve** the velocity is **diminished** and in **warmed nerve** it is **increased,** the limits of conductivity lying between 0°C. and about 50°C. Cooling a nerve to 0°C. (it is not frozen at this temperature because of the saline juices which bathe it) will sus-

pend conductivity completely; it will return, however, on warming. A temperature of about 50°C. kills the nerve.

**Narcotic drugs** such as chloroform, ether, chloral, alcohol, cocaine, applied locally, to nerve will block the impulse, i. e. prevent its passage; but conductivity will return when the drug is removed. This fact is taken advantage of by the surgeon in performing minor operations. If cocaine be applied to a nerve trunk supplying a certain area of skin, no impression from that area can reach the brain and give rise to pain.

The effect of gases and vapors on the excitability and conductivity of nerve is studied by the gas-chamber method. (Copy diagram). The action of two gases, $CO_2$ and oxygen, is interesting.

$CO_2$ IN SMALL AMOUNT, i. e. IN GREAT DILUTION, INCREASES THE IRRITABILITY AND CONDUCTIVITY OF NERVE FIBERS, BUT IN LARGER AMOUNT IT DIMINISHES BOTH AND ULTIMATELY KILLS THE NERVE.

**The relation of oygen** to the functional activity of nerve fiber is very important when considering the nature of the nerve impulse. IN AN OXYGEN-FREE ATMOSPHERE CONDUCTIVITY IS ENTIRELY LOST BUT IT WILL RETURN IF OXYGEN IS READMITTED. The fact that oxygen is essential would seem to point to the conclusion that the passage of a nerve impulse implies some chemical change.

Mechanical pressure on a nerve will also suspend its conductivity without permanently injuring the fibers provided the pressure is not excessive.

**Fatiguability of Nerve**— Can the excitability and conductivity of a nerve fiber be suspended by prolonged or excessive stimulation, i. e. can a nerve fiber be fatigued? The following experiment appears to answer this question:

Two nerve-muscle preparations from the same frog are arranged so that each nerve is stimulated alike with the interrupted current and each muscle lifts a weight of 30 grams. In one of the preparations (A) an area of the nerve between the point stimulated and the muscle is cooled so as to prevent the passage of an impulse, thus protecting the muscle; in the other (B) the muscle contracts and lifts the weight and in 10 or 15 minutes it will be completely fatigued. Now in A remove the block by raising the temperature and its muscle will contract. This shows that the nerve of A has not been fatigued although it was stimulated equally with that of B. It has thus been found that prolonged excitation, for hours, will not produce in nerve fibers any signs of fatigue.

This is not true of nerve cells, however; these quickly show signs of fatigue and microscopical changes of the nature of **chromatolysis** can be demonstrated in them as the result of stimulation and functional activity.

## Nature of the Nerve Impulse

Three theories have been advanced to explain the nature of the nerve impulse. 1. It may be **chemical** resembling somewhat the firing of a train of gun powder. The stimulus applied to the nerve may cause the explosion or breaking down of some unstable substance in the axis cylinder, the disturbance being propagated along the nerve as a progressive chemical change. It is necessary to assume here that the substance broken down is immediately rebuilt up, because a nerve fiber shows no signs of fatigue or exhaustion after stimulation with the interrupted current for hours. Two facts give support to this theory.

1. **Oxygen is essential,** as we have seen, for nerve conduction, and this would seem to indicate chemical change. 2. It has been shown by Tashiro that **$CO_2$ is produced** in nerve fiber, in increased amount, when it is stimulated. This again points conclusively to chemical change of a disintegrative nature, $CO_2$ being the final product of oxidation.

Certain other facts, however, do not appear to agree with the chemical theory. 1. **No heat,** in detectable quantity is produced in nerve fiber, and heat production is always associated with oxidative changes. 2. **Nerve fiber is unfatiguable.** It would appear that if the conduction of a nerve impluse depend on the decomposition of any substance stored in the fiber, this substance would, in the course of time, become exhausted.

2. It may be something of the nature of a **mechanical** vibration passing along the nerve fiber resembling a sound wave transmitted along a steel rod, for example. The fact that no heat is produced, and that fatigue cannot be induced seem to support this idea.

3. It may be something of the nature of an **electrical** change sweeping along the nerve fiber. This is a possibility but it has not been proved, and the reasons for and against it cannot be given, with advantage, in an elementary text-book.

## Nerve Degeneration

A nerve fiber cut off from its cell of origin undergoes degenerative changes since the cell acts as the trophic or nutritive center for the nerve fiber. This important fact was discovered by Dr. Waller in 1850 and hence is termed **Wallerian or secondary degeneration.** The degenerative changes in the nerve fiber are evident a few days after its section. The MYELIN of the medullary sheath BREAKS UP into fatty globules and ultimately DISAPPEARS; the AXIS CYLINDER also DISAPPEARS, but the NEURILEMMA REMAINS and acts as a scaffolding for the new axis cylinder which grows down from the central stump when the nerve degenerates.

When **regeneration** takes place the function of the nerve is restored, that is, motion or sensation returns, as the case may be.

If a nerve is accidentally torn or cut across, repair may be expected in time, but this time is greatly shortened if the surgeon unites the two ends of the divided nerve with a few stitches, because then the new axis cylinders will find their way more readily from the central end into the neurilemma of the peripheral part.

Wallerian degeneration furnishes a very important method of tracing the course of nerve fibers, particularly in the brain and spinal cord.

## CIRCULATORY SYSTEM

### Course of Blood in Circulation

The heart and blood-vessels form a closed system filled with blood. The mammalian heart is divided by a complete septum into **four chambers**—two auricles and two ventricles, right and left.

Starting from the **left ventricle** the blood passes into the **aorta,** then into the **smaller arteries** and then into the **capillaries.** From the capillaries it is collected into the **veins** and is finally poured into the **right auricle.** This is called the **greater or systemic circulation.**

From the **right auricle** the blood passes into the **right ventricle,** and from there to the **lungs** through the **pulmonary artery** which soon divides into two branches, one for each lung. In the lungs it passes through a second set of **capillaries,** is collected again by the veins and reaches the **left auricle** through the large **pulmonary veins,** four in number, two for each lung. This is known as the **lesser or pulmonary circulation.** From the **left auricle** it passes to the **left ventricle,** the point from which we started, thus completing the circulation.

The blood which goes to the stomach, intestine, pancreas and spleen, after passing through the capillaries of these organs, is collected by their veins which all unite to form a single large vessel called the **portal vein,** and through this it enters the liver where it is again driven through a set of capillaries—the **hepatic capillaries.** Finally it leaves the liver by the **hepatic veins** which join the **inferior vena cava** and so reaches the **right auricle.** This is termed the **portal circulation.** It will be noted that the blood of the portal circulation passes through TWO SETS OF CAPILLARIES.

A somewhat accessory circulation is that through the kidneys—the **renal circulation.** A part of the blood takes this course—from the aorta, through the renal arteries, capillaries and veins to the inferior vena cava.

**The lymphatic vessels** really form a part of the circulatory system. The lymph, which consists essentially of the fluid part of the blood that has passed through the capillary walls into the tissues, is collected by the lymphatic vessels, and after passing through lymph glands is poured into the blood by two large lymphatic vessels—the **right lymphatic duct** and the **thoracic duct** both of which open into the large veins in the root of the neck near the heart. (Copy diagram.)

As will be explained later, the blood travels much more slowly through the capillaries than it does through the arteries and veins,

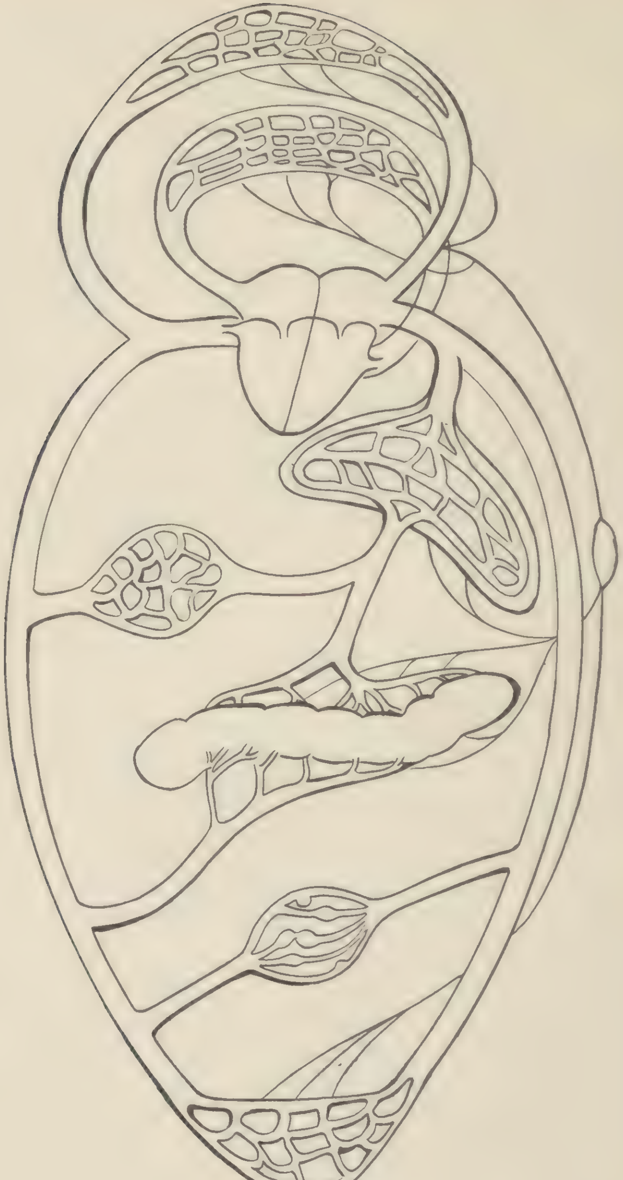


Fig. 4

and this gives time for the interchange of products between the blood and the tissues.

## THE HEART

The heart is a muscular pump whose rhythmical contractions force the blood to move in a circle. It is an organ somewhat pyramidal in shape, with the apex pointing downwards and to the left. It lies behind the sternum and ribs but it is almost entirely separated from the anterior chest wall by the lungs, only a small area remaining uncovered. In the adult it is about five inches long and 3½ inches across at its widest part. It weighs 9–10 ounces. It gradually increases in weight up to middle life and in old age it diminishes.

**Pericardium**—The heart is enveloped in a fibrous bag called the pericardium, which rests on the diaphragm. It is lined on the inside by **endothelium** which is reflected over the surface of the organ, thus two smooth surfaces are apposed—the **parietal** layer and the **visceral** layer of the pericardium—and this helps to diminish friction when the heart contracts. There is no actual space between the two layers in health, but if this lining becomes inflamed (pericarditis), serous fluid is poured out and accumulates, forming a real space.

**Endocardium**—Internally each of the heart cavities is also lined by a fibrous membrane covered by a single layer of flattened epithelial cells or ENDOTHELIUM; this is termed the endocardium.

**Myocardium**—Between the endocardium and the visceral layer of the pericardium, the muscular tissue is found; this is called the myocardium. In addition to heart muscle it contains blood-vessels, nerve cells and fibers, and some connective tissue.

The left ventricle is much thicker in the wall than the right; it is connected with the greater or systemic circulation and has much more work to do than the right.

The musculature of the auricles is separated from that of the ventricles by a RING OF FIBROUS TISSUE but a peculiar kind of muscular tissue, which is probably not contractile but only conductive, passes across this ring; it is called the auriculo-ventricular or A—V bundle, or the **bundle of His,** and it is believed to convey the stimulus from the auricles to the ventricles.

### Heart Valves

The heart valves are essentially folds of endocardium strengthened by fibrous tissue; they are smooth and strong. One set, the **auriculo-ventricular valves,** are placed between the auricles and ventricles; another set, the **semilunar valves,** are situated at the openings of the aorta and pulmonary artery into the left and right ventricles respectively.

There are TWO AURICULO-VENTRICULAR (A—V) VALVES, one between the right auricle and ventricle, usually called the tricuspid valve, and the other between the left auricle and ventricle, commonly known as the mitral valve.

**The tricuspid valve** has three cusp shaped flaps, as the name indicates, attached at their bases to the fibrous ring surrounding the A—V orifice, with their apices projecting into the ventricle. Attached to the ventricular aspect of these flaps are numerous fine tendinous cords—**the chordæ tendineæ**—whose function it is to prevent the flaps being shot into the auricle when the ventricle contracts. At the other end they are connected with muscular elevations on the inner wall of the ventricle known as the papillary muscles or **musculi papillares.**

**The mitral valve** on the left side of the heart is built on the same plan as the tricuspid, but it is much stronger and has **two cusps** instead of three. The papillary muscles on the left side are also better developed and more powerful than those on the right.

**Semilunar Valves**—The aortic and pulmonary openings from the left and right ventricles, respectively, are each guarded by three semilunar valves. The convex margin of each of these semilunes is attached to the fibrous ring around the opening while the concave free edge projects into the artery. When the valves are closed, by pressure on the arterial side, their thin edges are applied firmly to each other so that no blood gets through between them, the wrong way. Outside each of the flaps there is a bulging in the wall of the artery; this is called the **Sinus of Valsalva;** it forms a little pocket in the side of the vessel. There are three sinuses to each valve. The function of these sinuses is to prevent the valves from sticking to the wall of the vessel. When the blood is passing out of the ventricles, they permit of an eddy stream getting in behind the valves, and helping to close them the moment the axial stream is over.

The only difference between the aortic and pulmonary valves is that the former is the stronger.

## Coronary System of Vessels

The coronary arteries, right and left, arise from the base of the aorta and carry blood to nourish the heart wall. The smaller arteries end in capillaries, and these unite into veins which bring the blood back to the right auricle, through the coronary sinus. The coronary arteries are TERMINAL ARTERIES; they do not anastomose, and when one of their branches is blocked, the blood is completely cut off from the whole area supplied by that vessel. It is on this account that occlusion of one of the coronary arteries, by a blood clot or embolus, may be instantly fatal.

In the frog the heart wall is so thin and spongy that no special nutrient system of vessels is necessary.

### Openings in the Heart Chambers

The superior and inferior venæ cavæ both open into the right auricle and also the coronary sinus formed by the union of the coronary veins. The right auricle communicates with the right ventricle by the right A—V orifice guarded by the tricuspid valve. The pulmonary veins—usually four in number in man—open into the left auricle and this opens into the left ventricle through the left A—V orifice guarded by the mitral valve. There are no valves guarding the openings of the great veins at their entrance into the auricles.

### Action of Valves in Directing the Flow of Blood Through the Heart

If the heart were without valves the blood would simply flow to and fro and not in a circle.

Before the auricles contract blood is slowly flowing from the great veins into the auricles and from these into the ventricles, the A—V valves being open. When the auricles contract to expel their blood, it is driven into the ventricles which are thus forcibly distended. The axial stream may form a kind of eddy behind the flaps of the A—V valves and when it (the axial stream) has come to an end that moment the VALVES CLOSE, i. e. BEFORE THE VENTRICLES HAVE ACTUALLY BEGUN TO CONTRACT.

The ventricles then contract and in doing so stretch the A—V valves. When the pressure in the ventricles exceeds that in the great arteries the semilunar valves open, and the blood is propelled into the arteries—pulmonary and aorta. As soon as the blood flow from the ventricles is at an end the semilunar valves close, and the ventricles begin to relax, taking away the support from the valves behind. The blood tends to rush back into the heart, but encountering the now closed valves it is unable to do so. There is then a complete pause in the heart's action and the whole series of events is repeated.

Both auricles contract synchronously and both ventricles.

**Functions of Chordæ Tendineæ and Papillary Muscles**—When the ventricles contract the pressure in them rises suddenly, and the flaps of the A—V valves would be everted into the auricles if this were not prevented by the chordæ tendineæ which hang on to them. During their contraction, however, the apex of the heart approaches the base so that the chordæ tendineæ might still allow the cusps to pass into the auricles if it were not for the fact that the PAPILLARY MUSCLES, to which they are attached, CONTRACT AND SHORTEN AT THE SAME TIME. This shortening of the papillary

muscles COMPENSATES exactly for the upward movement of the apex and the chordæ tendineæ are still kept taut.

## Incompetent Valves and Regurgitation

An incompetent valve is one which permits the blood to flow in the wrong direction; this backward flow is known as **regurgitation.** If the ventricles are over distended the flap of the A—V valves do not come together and blood escapes backwards or regurgitates into the auricles. On account of the comparative thinness of its walls this is more liable to occur in the right ventricle than in the left.

It sometimes happens that the valves are roughened as the result of disease—endocarditis—and do not meet properly at the edges, thus permitting the blood to regurgitate. This condition may be found in any of the heart valves. It frequently follows acute rheumatism and it is permanent.

**Cardiac Hypertrophy and Compensation**—If there are defective valves and leakage backwards the tissues will not receive a sufficient supply of blood. This is quickly corrected, however, by the heart becoming thicker in the wall, i. e. undergoing hypertrophy, so as to pump more blood forwards and so make good the leakage. Persons may live in good health for many years with defective heart valves because of the power which the heart possesses of undergoing **hypertrophy** and providing **compensation.** It is only when this compensation fails, with advancing years, that symptoms appear.

## Heart Movements

**The rhythmical movements of the heart** may be conveniently studied by attaching the apex of a frog's heart to a **lever** which is made to record its movements on a **revolving drum.** The rhythm is sinus—auricles—ventricles—pause. The contraction wave begins in the sinus, in the frog's heart, then sweeps over the auricles and then on to the ventricle there being no intervening connective tissue band between the auricles and ventricle in the frog.

In the mammalian heart there is no sinus but the part that corresponds to it, termed the **sino-auricular node** or the node of Keith and Flack, is situated in the right auricle, near the entrance of the superior vena cava. It is at this point that the contraction wave begins in the human heart; it sweeps over the auricles, then passes on to the ventricles through the A—V bundle before described, since there is no continuity of muscular tissue between the auricles and ventricles except through this bundle.

**Effect of Temperature on Heart Beat**—The effect of heat and cold can be conveniently studied on this frog's heart preparation. **Heat accelerates** the rate and diminishes the force of the beat

and **cold slows** the rate and augments the force. The rapid heart of fever is due, in part, to the high temperature of the blood.

## The Cardiac Cycle

If a tracing be taken from the heart of a turtle, one lever can be attached to the auricles and another to the ventricle, each recording its movements separately on a revolving drum. If the writing points be arranged on the same vertical line, one above the other, it will be seen that the auricular contraction is over before the ventricular contraction begins, and after that is over there is a pause until the next auricular contraction. THIS SEQUENCE OF EVENTS, FROM THE BEGINNING OF ANY ONE EVENT TO ITS NEXT BEGINNING, CONSTITUTES A **cardiac cycle. Contraction** of heart muscle is termed the **systole** and **relaxation** the **diastole,** so that we have the auricular systole followed by the auricular diastole and the ventricular systole by the ventricular diastole.

The same kind of record would be obtained from the human heart, if it were possible to attach levers to the auricles and ventricles, but the events would succeed each other much more quickly, that is, the cardiac cycle would be shorter.

## Apex Beat

The apex of the heart rests against the chest wall about the fourth or fifth intercostal space; its impact against the chest wall is known as the apex beat. This may be recorded by a **cardiograph,** an apparatus consisting of two TAMBOURS, one of which is applied to the chest wall at the spot where the apex beat can be best felt with the finger (usually in the 4th intercostal space about one inch to the left side of the sternum), and the other attached to a lever which writes on a revolving drum. When the chest wall advances (driven forward by the impact), air is driven out of the receiving tambour on the chest into the transmitting tambour on the stand, so that the lever is elevated; when the chest wall recedes, air moves from the transmitting to the receiving tambour and the lever falls.

[The tambour is an instrument, now much used in physiology, first devised by Marey of Paris. It consists of a flattened brass box closed on one side with a thin rubber membrane, and provided with a side tube to which rubber tubing can be attached. To the center of the membrane is glued a small metal disc and on this rests a lever which rises when air enters the box and causes the membrane to bulge, and falls when air escapes from the box. Tambours are most frequently used in pairs, the one RECEIVING the movement, the other TRANSMITTING IT].

## Heart Sounds

"There are two audible sounds produced by the heart during each cardiac cycle; they are termed first and second, or long and short, or systolic and diastolic. Both are musical notes of low pitch; the first is dull, the second is sharp and of higher pitch. The sounds may be imitated by pronouncing the words, lūbb-dŭp, at the proper pitch.

**The first sound** begins the moment the ventricles begin to contract but it dies away before the contraction is over; it is succeeded by a short period of silence. **The Second sound** begins the moment the ventricle begins to relax, i. e. at the beginning of the pause (see diagram); it is shorter than the first and is succeeded by a long silence.

**Causes of Heart Sounds**—The SECOND SOUND is due to the vibration resulting from the sudden stretching of the semilunar valves—NOT TO THEIR CLOSURE. It is **entirely valvular** and this can be proved by the following experiments:

1. If a wire, with a hook on the end of it, be pushed into the aorta and another into the pulmonary artery of an anæsthetized animal, e. g. a horse, and the flaps of the semilunar valves held aside, the second sound disappears and is replaced by a murmur.

2. If the heart be entirely emptied of blood by clamping the superior and inferior venæ cavæ, it will continue to beat for a short time, but the second sound will disappear completely. This proves that it is not muscular but purely valvular.

3. A similar sound can be produced in the excised and dead heart, by tying a long glass tube into the aorta and filling it with water. If the ventricle be cut away and the valves held open for a moment and then allowed to be closed by the pressure of the water, a sound is produced by the stretching of the valves similar in character to the second heart sound.

The second sound is produced at both the aortic and pulmonary valves, and there are not two second sounds because in health both sets of valves are stretched at the same time. The aortic valve produces more of the second sound than the pulmonary because it is three times as strong and is more powerfully stretched by the greater blood pressure in the aorta.

**The first sound** has two causes. The stretching of the A—V valves is the first and most important cause, and the second is the contraction of the muscular fibers of the ventricles, but this is not so evident as the valvular part. The experimental proofs are not so strong as in the case of the second sound; they are as follows:

1. If the superior and inferior venæ cavæ be clamped, the heart soon empties itself, and the A—V valves can no longer be stretched,

but the first sound does not disappear; it loses much of its musical character, however, and becomes a low rumbling noise, such as might be produced by contracting muscle.

2. If the apex of the heart is cut off, allowing the blood to escape, so that there can be no pressure in the ventricles, and consequently no stretching of the A—V valves, it continues to beat for a few minutes, and there is still heard this low rumbling noise representing the first sound.

In the **first sound,** then, there are **two factors**—1, **stretching of the A—V valves;** 2, **contraction of the ventricular muscle.**

The character of these sounds is an important guide to the physician regarding the condition of the heart. For example, a loud second sound indicates high blood pressure, and a loud first sound points to a powerfully contracting heart, while a feeble first sound shows that the heart is weak, etc."

**Heart Murmurs**—In valvular disease the heart sounds are replaced by murmurs. For example, if the A—V valves are roughened so that they can't close properly, when the ventricles contract the blood will flow backwards into the auricles, and this rushing of fluid over the roughened valves will cause, not a musical sound such as is produced by the vibration of the closed valves, but a noise which in medicine is called a **murmur.** This would be a **systolic murmur** because it occurs during the **ventricular systole.** Again, if the semilunar valves are involved, the blood rushing out into the arteries during the ventricular contraction will produce a systolic murmur and another murmur, **diastolic** in time, will be caused by the blood rushing back again into the ventricles, during their relaxation, through the incompetent valves. Here we will have a systolic murmur succeeded by a diastolic.

**Points on the Chest Wall where the Heart Sounds are Best Heard**—The heart sounds may be heard perfectly well by placing the ear against the chest, but it is more convenient to use a **stethoscope.** They are not most audible over the valves where they are produced, but at the points where the heart or great vessels come nearest to the chest wall. The aortic element of the second sound is best heard by placing the chest piece of the stethoscope on the second right costal cartilage, at its junction with the sternum. This is explained by the fact that the aorta, after it leaves the left ventricle, arches upwards and to the right and comes closest to the surface at this point. The pulmonary element of the second sound is most audible over the second intercostal space, close to the left edge of the sternum. The mitral element of the first sound is best heard at the apex beat and the tricuspid element close to the left border of the sternum, in the 4th intercostal space.

### Work Done by Heart

It is estimated that each ventricle of the heart ejects about 100 c.c. of blood at each beat against the resistance of the blood pressure in the arteries and that in doing this it performs 285 gram-meter units of work; that is, the force exerted by the heart at each beat is capable of raising 285 grams 1 meter high. Knowing that the heart in the human subject beats 72 times per minute, the total work for the 24 hours is calculated to be 29,558,800 gram-meters.

## NERVE SUPPLY OF THE HEART

The heart beats automatically—it will continue to beat for hours, under proper conditions, when entirely removed from the body—but its action is controlled by two nerve centers situated in the medulla oblongata, viz.—the **cardio-motor centre** and the **cardio-inhibitory center.**

[By a nerve center is meant a group of nerve cells situated somewhere in the central nervous system, i. e. in the brain or spinal cord. The medulla oblongata is the lowest division of the brain, that next to the spinal cord.]

**Course of Impulses from Cardio-motor Center to Heart**—There are **three superimposed sets of neurons** on this path. The first arises in the c.—m. center in the medulla oblongata and ends in the grey matter of the spinal cord in the upper thoracic region; the second leaves the cord through the anterior roots of the 2d, 3d, and 4th thoracic nerves and ends in the inferior cervical ganglion; the third passes from this ganglion to the heart. There is in this series one **central** set of neurons, one **preganglionic,** and one **postganglionic.**

[All nerve fibers between the spinal cord or brain and the autonomic ganglia are termed preganglionic fibers and all between the ganglia and the tissue in which they end are called postganglionic fibers.]

On this path there are **two cell stations,** one in the grey matter of the spinal cord and another in the inferior cervical ganglion.

Stimulation of these fibers, at any point in their course, leads to an acceleration of the heart rate and sometimes also to an augmentation in the force of the beat. For this reason it is believed that there are two kinds of fibers which pass from the c—m. center to the heart, viz.:—**accelerator fibers** and **augmentor fibers.**

### Course of Impulses from Cardio-inhibitory Center to Heart

On this path there are **two superimposed sets of neurons.** The first joins the vagus or 10th cranial nerve, right and left, and passes through that to the heart; the second is situated in the

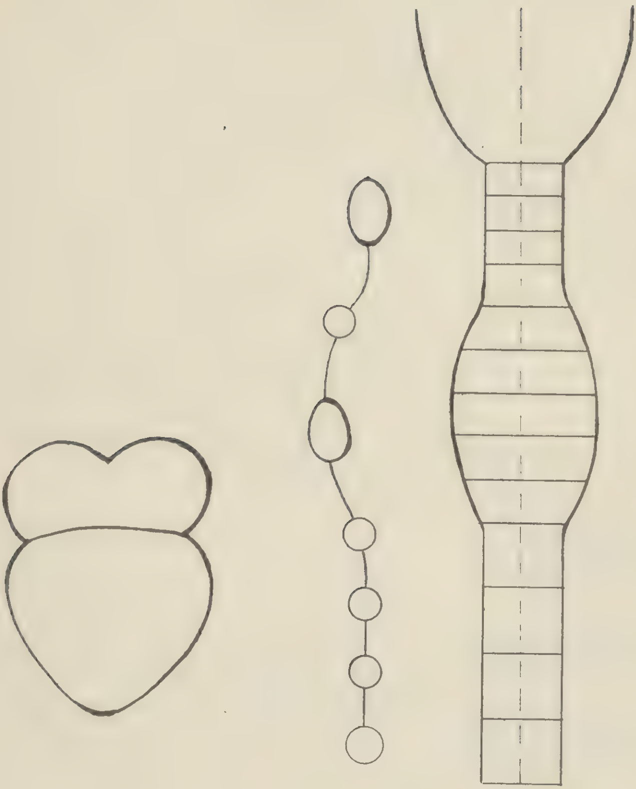


Fig. 4

heart wall itself. Groups of nerve cells, forming the **intracardiac ganglia,** are found scattered amongst the muscular fibers; these give origin to short nerve fibers which end in the heart muscle. The second set of neurons is formed of these intracardiac cells and fibers. In this path there is **one cell station,** that in the heart wall.

**Effect of Dividing Vagus Nerve on Heart Beat**—If one vagus be divided in the neck, above the point where the heart fibers leave it, the **heart beats faster;** if then the other vagus be cut it beats faster still. This proves that, since the heart beats faster when it is cut off from the c—i. center, normally this center must be in a state of **tonic activity,** i. e. always in action sending down impulses to check the heart rate.

The cardio-motor center is probably also in tonic activity although the fact is not so easily demonstrated.

**Effect of Stimulating Peripheral End of Divided Vagus**—When the peripheral (heart) end of the cut vagus is stimulated the **heart is slowed** and if the stimulus is strong enough it is **stopped** altogether. This proves that the vagus nerve contains **inhibitory fibers** for the heart.

**Action of Atropin and Nicotin on the Heart**—The action of two drugs much used in physiological investigations, viz.—atropin and nicotin, is interesting in this relation. If **atropin** be administered to an animal the heart rate is greatly **increased,**—just as much, in fact, as it would be if both vagi nerves were divided. This drug has the property of paralyzing the terminations of the second set of neurons in the heart muscle and so the impulses constantly being sent down from the c—i. center, through the vagi, never reach the heart. For the same reason, if the peripheral end of the divided vagus be stimulated, after giving the atropin, no effect is produced on the heart rate; it is not slowed or stopped.

Nicotin has the same effect as atropin but it acts in a different manner. **Nicotin paralyzes the synapses** between the first and second neurons on the inhibitory path.

**Effect of Stimulating Central End of Divided Vagus**—The vagus nerve carries **afferent** or sensory fibers from the heart to the brain as well as efferent (inhibitory) fibers from the brain to the heart. When the central end is stimulated, therefore, these afferent fibers will be excited and this will cause either a slowing of the heart rate **reflexly** or an acceleration of it. It may be impossible to predict which action it will have before hand; for example, if the impulses which pass up inhibit the activity of the c—i. center of the other side, the heart rate will be increased; if they excite the c—i. center it will be decreased. Again, if they excite the c—m. center the heart will beat faster; if they inhibit its activity it will beat slower. By inhibiting the one center and exciting the other it is possible to get no alteration at all in the heart rate.

This experiment shows the importance, in studying the function of a nerve, of first dividing it before stimulating. For example, if the intact vagus nerve had been excited and heart slowing obtained it would be impossible to say whether the action were reflex or direct.

**Innervation of Heart in Frog**—In the frog the arrangement is peculiar. The accelerator and augmentor fibers join the vagus in the neck and are carried to the heart along with the inhibitory fibers, consequently, when the peripheral end of the cut vagus is stimulated the effect may be acceleration or inhibition depending upon which set of fibers is the more susceptible to the stimulus.

**Influence of Higher Brain Centers on Heart Rate**—The cardio-inhibitory and cardio-motor centers are affected reflexly by conditions at the periphery, but they are also under the control of the higher brain centers in the cerebrum, particularly the emotional centers. For instance, a sudden fright or surprise may cause the heart to beat faster (palpitation), or it may cause slowing or stoppage of the heart and fainting or even death, according as the impulses being showered down from the strongly excited emotional centers affect the c—m. center or the c—i. center. WE HAVE NO POWER VOLUNTARILY, HOWEVER, EITHER TO INCREASE OR TO SLOW THE HEART RATE.

## NEUROGENIC AND MYOGENIC THEORIES OF HEART BEAT

1. **Neurogenic Theory**—When nerve cells were discovered in the heart itself, it was believed that these were responsible for the heart beat. The impulses were supposed to originate in these nerve cells and to be conducted, through the short nerve fibers, to the heart muscle, causing it to contract. This is the NEUROGENIC THEORY.

2. **Myogenic Theory**—Then it was shown by Gaskell that strips taken from the ventricle of the turtle's heart, containing neither nerve cells nor nerve fibers, if attached to a lever and immersed in Ringer's fluid, will beat rhythmically for hours. Also in the developing chick, at a very early stage, the heart can be seen to beat long before any nerve tissue has grown into it. For these and other reasons it is now held by most physiologists

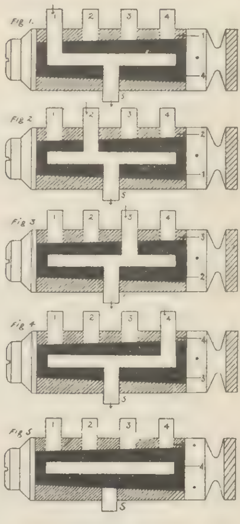


Fig. 5

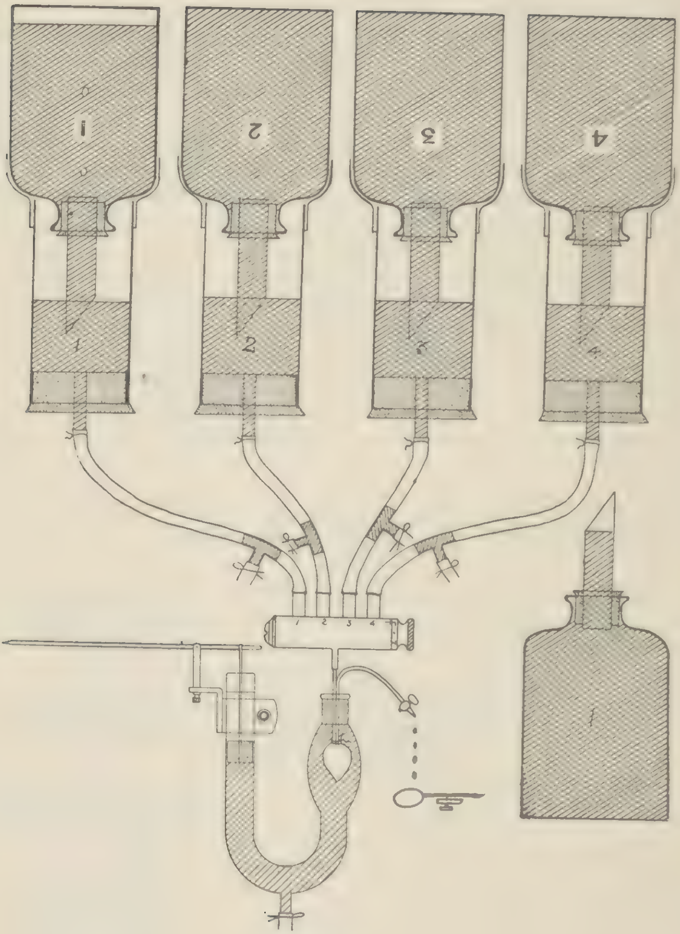



Fig. 6

that the contraction starts in the muscle itself, without any stimulus received from the nerve cells. This is the MYOGENIC THEORY.

**The Inner Stimulus**—Neither the neurogenic nor the myogenic theory, however, explains the rhythmicity of the beat. It is not enough to say that this is a property of heart muscle. Something must excite the nerve cell or the muscle fiber and that must be periodic in its application. The INNER STIMULUS that causes the muscle to contract has been looked for in the blood and there is some reason to believe that it is furnished by the **calcium and potassium** ions which may be set free in this fluid. Experiments on the frog's heart carried out with Schafer's plethysmograph appear to throw light on the question.

**Schafer's Frog Heart Plethysmograph**—If an opening be made in the auricles of a frog's heart and a two way cannula introduced into the ventricle, through this opening, and tied in by a ligature passed around the A—V junction, and if Ringer's fluid be allowed to flow into the ventricle, through one limb of the cannula, from a height of 3 or 4 inches and after distending the ventricle flow out at the other limb, the preparation will beat rhythmically as the frog's heart does in the body. The ventricle is being **perfused** with a fluid (Ringer's) which is practically the same as the frog's blood plasma minus its organic constituents,—a solution of the inorganic salts of sodium, calcium and potassium in the same proportion as they exist in the plasma.

| Ringer's Fluid | | Locke's Fluid | |
|---|---|---|---|
| Na Cl | 0.700% | Na Cl | 0.900% |
| K Cl | 0.030 | K Cl | 0.042 |
| Ca $Cl_2$ | 0.025 | Ca $Cl_2$ | 0.024 |
| H Na $CO_3$ | 0.003 | H Na $CO_3$ | 0.020 |
| | | Dextrose | 0.100 |

If now the ventricle be introduced into the expanded bulb of a U-tube filled completely with Ringer's solution and having a float, with a lever attached, in the open limb, then, when the heart expands in diastole, the volume will increase, the float will rise and the writing point of the lever will descend; when the heart contracts in systole, the volume will diminish, the float will fall and the lever point ascend. The apparatus is termed a **plethysmograph** or volume writer and the record obtained on a revolving drum a **plethysmogram.** In a good preparation the heart will continue to beat for hours, on Ringer's fluid alone, which contains only **inorganic** salts.

If a slight excess of **calcium** chloride be added to the fluid the systole will become more powerful and, by-and-bye, the heart will stop with the muscle **completely contracted** and unable to relax. At this stage, if the preparation be fed with Ringer's solution con-

taining a slight excess of **potassium** chloride, it will start to beat again, gradually becoming relaxed with the diastole more and more prolonged until at last it stops in diastole, i. e. in **complete relaxation.** Therefore, calcium has the power of stimulating heart muscle and potassium of inhibiting it.

**Calcium-Potassium Ion Theory of Inner Stimulation**—Suppose that during diastole **calcium** ions are set free, when they reach a certain concentration the muscle will be excited and the heart will pass into **systole.** Suppose that during systole **potassium** ions are set free, when these reach a certain concentration the contraction will be inhibited, and the heart will pass into **diastole.** It is conceivable that in this way the heart is kept going between calcium stimulation and potassium inhibition, showing the alternate phases of systole and diastole.

By the plethysmographic method records may also be obtained from the isolated mammalian heart (even the human heart), but here Locke's solution, containing sugar, must be used as the perfusing fluid; it must be super-saturated with oxygen, and it must be kept warm.

### Physiological Properties of Heart Muscle

Heart muscle differs from skeletal (voluntary) muscle in three respects: 1. A minimal stimulus causes a maximal contraction; this is known as the "ALL OR NOTHING" phenomenon. Recent investigation has shown that the same kind of response is given by striated muscle. 2. Heart muscle CANNOT BE TETANISED because of its long refractory period. 3. Heart muscles show RHYTHMICAL CONTRACTION.

These properties of heart muscle may be studied on a frog's heart which has been brought to a standstill by a **Stannius' ligature.** If a thread be tied tightly around the sino-auricular junction the heart will stop beating for a considerable time. The reason assigned for this is that the contraction wave, which starts in the sinus, cannot get across the ligature and so never reaches the auricles and ventricle. By-and-bye, however, the auricles themselves will initiate a contraction wave and the heart will start again.

While the heart is quiescent, under the Stannius' ligature, it may be attached to a lever writing on a revolving drum and stimulated by electrical shocks just like the gastrocnemius muscle.

### Electrical Changes in the Heart

The contraction of the heart muscle, like that of skeletal muscle, is accompanied by an electrical change. The part in contraction becomes negative to the parts at rest and this gives rise to a current of action which can be demonstrated and recorded by a string galvanometer. The record is known as the **electrocardiogram.** If the heart is diseased the electrocardiogram will be abnormal and this method is now extensively used by physicians in diagnosing heart affections.

## BLOOD-VESSELS

These are the arteries, capillaries and veins.

**The arterial system** begins at the left ventricle of the heart in a large vessel, the **aorta.** This turns abruptly downwards (arch of aorta), and passes through the thorax and abdomen, as a single large vessel (the thoracic and abdominal aorta) giving off many branches, large and small, in its course. In the abdomen it divides into the two **common iliac arteries** which carry the blood to the lower limbs. Just after leaving the heart it gives off three large branches—the innominate, the left common carotid and the left subclavian arteries—which carry the blood to the head, neck and upper limbs. The arteries divide and subdivide into smaller and smaller branches, the most minute being termed the **arterioles,** and these become continuous with the capillaries.

The arteries, generally speaking, are placed more deeply than the corresponding veins and are protected from pressure and other dangers, but there are many exceptions to this rule. In most situations their branches anastomose freely with the branches of other arteries, so that if one trunk is blocked, a collateral circulation is easily established. In certain organs, e. g. the brain and the heart, etc., the arteries are TERMINAL, i. e. their branches do not anastomose or communicate with other arteries, and the consequence of obstruction has already been mentioned in the case of the heart.

On account of their elastic walls which recoil on the blood and squeeze it out into the veins, in the dead body they are found empty, and so before the time of Harvey they were believed to contain air; hence the name artery or air pipe.

**Capillaries and Veins**—The capillaries, after a short course through the tissues, unite to form the smallest venules and these to form larger veins, until ultimately two big venous trunks are formed, the **superior** and **inferior venæ cavæ,** through which the blood is brought back to the heart. In medium and larger sized vessels the tributaries of the veins correspond in a general way, to the branches of the arteries.

Veins can easily be distinguished from arteries by the thinness of their walls and by the fact that they contain **valves**—all except the smallest and the largest—which the arteries do not. The vein is also larger in calibre than the corresponding artery at the same distance from the heart.

## Structure of Arteries and Veins

There are three coats—outer, middle and inner.

**The outer coat** consists of connective tissue containing an admixture of white and yellow elastic fibers, the latter arranged in a network.

**The middle coat** is made up mainly of **non-striped muscle** mixed with some elastic and white fibrous tissue. The muscle fibers run transversely to the long axis of the vessel, i. e. they are arranged circularly so that when they **contract** the vessel is **constricted.**

**The inner coat** is formed of a layer of elastic tissue termed the INNER ELASTIC LAMINA which in many situations is fenestrated. The inner lining of the vessel consists of a single layer of delicate ENDOTHELIAL CELLS which form a smooth surface for the blood to flow over and thus diminishes friction. Between the internal elastic lamina and the endothelial lining is some fine connective tissue.

In the veins the outer and middle coats are thinner than in the corresponding arteries, but otherwise the structure is the same, except for the presence of valves in the veins as already mentioned.

**Valves in Veins**—These have the same general structure as the semilunar valves of the heart. They consist of a fold of endothelium strengthened by connective tissue. They are arranged in pairs, the one opposite the other, and their free margins are directed towards the heart so that the blood is prevented from flowing backwards. Any pressure on the veins, such as might be caused by the contraction of muscles, will always cause the blood to move forwards, towards the heart, because of these valves. The position of these valves in the superficial veins of the forearm and back of hand can easily be made out by compressing the arm above to prevent the venous flow, when they will stand out as little swellings or knots through the skin.

**Structure of Capillaries**—If we trace the course of the large arteries down to the capillaries we find that the outer coat becomes thinner and thinner and finally disappears; the middle layer also becomes reduced and, in the smallest arteries, consists only of a single layer of circular muscle fibers which disappears entirely at the capillaries. The elastic membrane of the inner coat also disappears until, at the capillaries, nothing is left but the single layer of endothelial cells.

All the arteries are elastic (because of the yellow elastic fibers) and contractile (because of muscle), but the contractility is most marked in the smaller arteries, the elasticity in the larger. The capillaries are elastic but not contractile since they contain no muscle fibers.

## INNERVATION OF BLOOD-VESSELS

The muscular coats of the vessels, particularly the smaller arteries or arterioles, are supplied by two sets of nerve fibers—**vaso-constrictor** (commonly called vaso-motor) and **vaso-dilator** fibers, the one excitatory, the other inhibitory, as in the heart.

**The vaso-constrictor (or vaso-motor) center** is situated in the medulla oblongata, and impulses traveling down from this center stimulate the muscle fibers to contract, and so **constrict** or narrow the lumen of the vessels.

**Course of Impulses from Vaso-Constrictor Center to Blood-vessels**— These impulses travel over **three sets of neurons** as in the case of the cardio-motor fibers,— **central, preganglionic** and **postganglionic,** adopting the nomenclature of Langley. The **two cell stations** are situated in the grey matter of the spinal cord and in the autonomic ganglia respectively. The preganglionic fibers leave the cord through the anterior roots of all the spinal nerves from the **second thoracic to the second lumbar** inclusive. There are other regions of the central nervous system from which vaso-constrictor fibers come off but this is the chief one.

**A vaso-dilator center** is believed to exist but it has not been located with certainty.

Both vaso-constrictor and vaso-dilator nerve fibers were discovered by Claude Bernard.

**Claude Bernard's Experiment** which led to the discovery of the vaso-constrictor fibers was as follows: On examining the ear of a rabbit he observed that there were **rhythmical changes** in the blood vessels; the ear would become pale, owing to the constriction of the central artery and its branches, and after one or two minutes, it would become flushed again. He then cut the **sympathetic** (autonomic) nerve in the neck and found that after this, the vessels remained **permanently flushed,** and the temperature of the ear rose. He next **stimulated the peripheral (ear) end** of the divided nerve and found that the ear became **pale** again and remained so as long as the stimulus was applied.

The inferences to be drawn from this experiment are, first, that there are fibers in the cervical sympathetic nerve stimulation of which produces **constriction** of the blood-vessels of the ear on that side, and second, that the nerve center from which the impulses come that cause this constriction is in **tonic activity.** We now call this the vaso-constrictor (or vaso-motor) center and know that it is located in the medulla oblongata. Prior to this discovery of Claude Bernard the existence of such fibers, in any part of the body, was unknown.

Claude Bernard was also the first to demonstrate the existence of vaso-dilator nerve fibers. He did this by an experiment on the

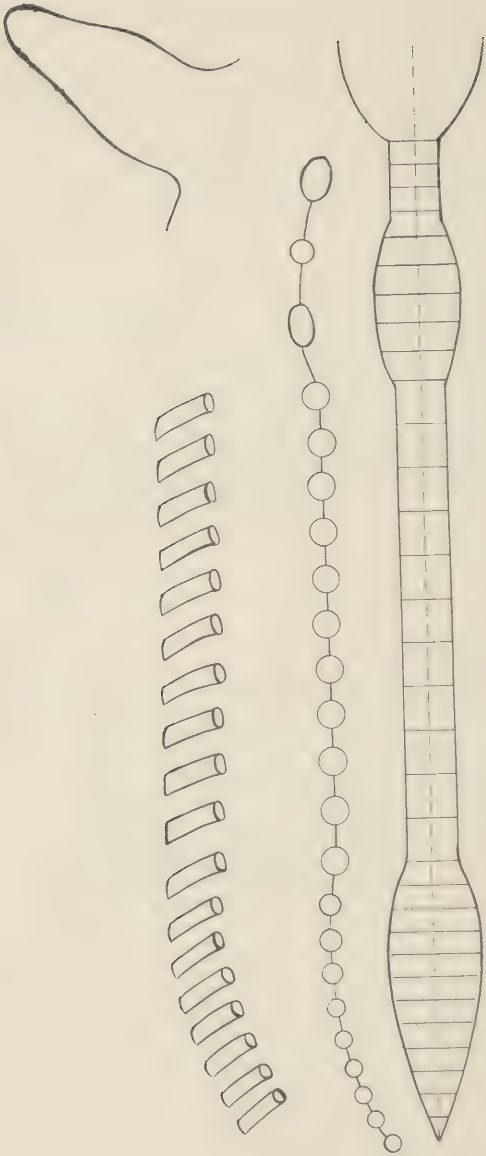


Fig. 7

submaxillary gland. This gland, which is situated under the lower jaw, is supplied by two sets of fibers one of which reaches it through the **cervical sympathetic** nerve and the other through the **chorda tympani,** a branch of the 7th cranial nerve. Bernard cut the chorda tympani and observed no change in the blood supply of the gland, but when he stimulated the **peripheral** (gland) end of the divided nerve, the gland became flushed at once indicating **dilation** of the bloodvessels.

The conclusions to be drawn from this experiment are, first, that the chorda tympani nerve contains vaso-dilator fibers, and second, that the VASO-DILATOR CENTER IS NOT IN TONIC ACTIVITY.

Stimulation of the cervical sympathetic nerve leads to a blanching of the gland, indicating constriction of the bloodvessels, while section of this nerve causes a permanent flushing, with the disappearance of rhythmical changes, showing that the vaso-constrictor center is in tonic activity.

**General Statement** based on above experiments. The VASO-CONSTRICTOR CENTER is always in a state of TONIC ACTIVITY maintaining vascular tonus. That is to say, impulses proceeding from the vaso-constrictor center, in the medulla oblongata, are constantly being showered down on the non-striped muscle fibers which form the middle coat of the arteries, particularly the arterioles, maintaining them in a semi-contracted condition and so keeping the vessels to some extent constricted. The strength of these impulses varies from time to time, and consequently so does the degree of constriction of the vessels. This variation is the cause of the rhythmical changes in the calibre of the vessels, as seen, for example, in the rabbit's ear.

There is NO EVIDENCE to show that the VASO-DILATOR CENTER is in TONIC-ACTIVITY, Vaso-dilation is the result of an inhibitory action on the vaso-constrictor fibers. In the case of the heart we saw that both the cardio-motor and cardio-inhibitory centers were in tonic activity, the latter more distinctly so than the former, however.

**Reflex and Central Stimulation of Vaso-Motor Centers**—Both the vaso-constrictor and vaso-dilator centers can be excited REFLEXLY by impulses reaching them from the periphery. In this respect they resemble other nerve centers; all nerve centers are reflex and depend for any change in activity on impulses reaching them from the periphery or from the higher brain centers. **Cold** applied to the skin will cause it to turn **pale;** impulses pass up to the vaso-constrictor center from the skin through the nerves that convey cold impressions; these excite the cells of the vaso-constrictor center reflexly and lead to a constriction of the bloodvessels of the skin and so to blanching. The application of **heat** has the opposite effect, i. e. it leads to vaso-dilatation and **flushing** of the

skin. This may be brought about in two ways, however; it may be caused by either stimulation of the vaso-dilator center or inhibition of the vaso-constrictor center.

As in the case of the heart so in the bloodvessels, their centers are under the control of the higher brain centers. The emotion of **shame** leads to BLUSHING due to dilatation of the vessels of the skin of the face, neck and ears, brought about by inhibition of the vaso-constrictor center or excitation of the vaso-dilator center, the impulses coming, this time, from above and not from the outside. Fear, on the other hand, leads most frequently to paling of the face due to vaso-constriction.

**Resumé**—The heart and blood-vessels are connected with the medulla oblongata by accelerator (and augmentor) and by inhibitory fibers (heart), and by vaso-constrictor and vaso-dilator fibers (bloodvessels). Nerve centers, situated in the medulla oblongata, are acted upon by impulses reaching them through afferent fibers from the skin and deeper tissues and organs, and also by impulses from the higher brain centers. The heart and blood vessels are capable of being affected reflexly through these centers by excitation of afferent nerves and also by emotional states. For instance, any influence which excites the cardio-inhibitory center or inhibits the cardio-motor center will produce slowing or stoppage of the heart; any influence which excites the cardio-motor center or inhibits the cardio-inhibitory center will lead to acceleration of the heart rate. Similarly, excitation of the vaso-constrictor center, reflexly or from the higher centers, will produce constriction of the arterioles and paling of the skin, etc., while inhibition of the vaso-constrictor center or excitation of the vaso-dilator center will cause dilatation of the peripheral vessels and flushing of the skin, etc.

## BLOOD PRESSURE

**The blood pressure** may be defined as the force with which the blood tends to escape from the vessels. It depends on the RELATION BETWEEN THE INFLOW AND OUTFLOW OF BLOOD IN THE VASCULAR SYSTEM, that is, between the force of propulsion represented by the heart's action and the force of resistance represented by the friction between the blood and the vessel walls.

The greater the length of the vessel wall the larger is the rubbing surface and the more is the resistance, therefore, the blood pressure is much greater in the arteries, near the heart, than in the veins. When the smaller arteries contract the friction in them increases, first because the ratio of the rubbing surface to the mass of blood passing through is increased, and second because the velocity is

greater. The normal variations in blood pressure are due mainly to changes in the calibre of the arterioles.

Poiseuille's schema to show fall in pressure from arteries to capillaries and veins demonstrated.

**Blood Pressure in Arteries, Capillaries and Veins**—The blood pressure is HIGHEST IN THE ARTERIES, LOWER IN THE CAPILLARIES AND LOWEST IN THE VEINS, and in the GREAT VEINS near the heart it is NEGATIVE owing to the suction action of the lungs which draws the blood out of the veins into the right side of the heart. The pressure does not fall uniformly, however, as it does in Poiseuille's schema. It is at its maximum in the aorta near the heart, diminishes slightly in the larger arteries and then falls suddenly in the arterioles so that the pressure in the capillaries beyond the arterioles is comparatively low.

**Methods of Measuring and Recording Blood Pressure**—It should be kept in mind that when we talk of blood pressure, without any qualification, ordinarily, we mean the pressure in the larger arteries, that is, arterial blood pressure.

**The blood pressure was first measured by the Rev. Stephen Hales** (1732). The method he adopted may be described in his own words:

"In December I caused a mare to be tied down alive on her back; she was fourteen hands high, and about fourteen years of age, had a Fistula on her Withers, was neither very lean, nor yet lusty. Having laid open the left crural artery about three inches from her belly, I inserted into it a brass pipe, whose bore was one-sixth of an inch in diameter; and to that, by means of another brass pipe which was fitly adapted to it, I fixed a glass tube, of nearly the same diameter, which was nine feet in length. Then untying the ligature on the artery, the blood rose in the Tube eight feet three inches perpendicular above the level of the left Ventricle of the heart. But it did not attain to its full height at once; it rushed up about half way in an instant, and afterwards gradually at each Pulse twelve, eight, six, four, two and sometimes one inch. When it was at its full height, it would rise and fall at and after each Pulse two, three, or four inches; and sometimes it would fall twelve or fourteen inches, and have there for a time the same Vibrations up and down at and after each pulse, as it had, when it was at its full height; to which it would rise again, after forty or fifty Pulses."

In this experiment of Hales the pressure in the artery, at the point where the tube was inserted, was measured by the height to which the blood rose in the tube.

In Hale's method there are two drawbacks; first the TUBE IS TOO LONG and unwieldy, and second the BLOOD CLOTS VERY QUICKLY when it escapes into the tube.

Two improvements were made by Poiseuille who SUBSTITUTED MERCURY FOR BLOOD and thus reduced the length of the tube 13.6 times, and who also used a solution of SODIUM CARBONATE between the blood and the mercury to DELAY THE BLOOD CLOTTING.

**Kymograph**—The method was further perfected by Carl Ludwig who placed a float on the top of the mercury, connected with a vertical rod and bearing a writing style which was made to record its movements on a revolving drum. This is now known as the LUDWIG KYMOGRAPH.

**Method of Recording the Blood Pressure with Ludwig's Kymograph**—To begin with, a positive pressure must be produced in the system by means of a PRESSURE BOTTLE (see diagram), and this should be a little in excess of what the blood pressure in the artery is expected to be,—in the case of a dog, from 5 to 6 inches of mercury.

The animal, dog say, is now anæsthetized with ether, one of the common carotid arteries is exposed in the neck and a CANNULA (glass tube) tied into it. Before the artery is opened a small clamp must be placed on it, between the heart and the opening, to prevent the escape of blood. The cannula, filled with a solution of SODIUM CARBONATE, is then attached to a MERCURIAL MANOMETER (U-tube) by a thick walled rubber tube, and the clamp removed from the artery. If the positive pressure in the system is equal to or slightly above that in the artery, no blood will escape and so will not be liable to clot in the cannula containing the sodium carbonate solution. The WRITING STYLE, attached to the open limb of the manometer, is now brought into contact with the MOVING SURFACE and a record of the blood pressure obtained. Simultaneously a TIME TRACING can be taken underneath. The blood pressure in the carotid artery of the dog lies usually between 5 and 6 inches of mercury.

A typical blood pressure tracing or kymogram so obtained from an anæsthetized animal will show THREE SETS OF WAVES. The smallest represent the HEART BEATS; next in size are the RESPIRATORY WAVES (pressure rises during inspiration and falls during expiration), while the largest, very irregular, are due to CHANGES IN THE ACTIVITY OF THE VASO-CONSTRICTOR CENTER whereby the blood pressure, in normal conditions, is constantly undergoing slight variations.

This instrument (Ludwig's Kymograph) is not perfect, however. There is an objection to mercury as a medium for transmitting the pressure because of the great momentum which it acquires in the oscillations due to the heart beats so that the finer changes in pressure in the artery are lost.

**Hürthle's Manometer**—Hürthle has devised a simple apparatus which, to a large extent, overcomes this objection. It consists of

a small METAL BOX covered with a RUBBER MEMBRANE to which a very light LEVER is attached. This is filled with sodium carbonate solution and connected, through a cannula, with the blood-vessel in place of the mercurial manometer. When the pressure in the artery increases the membrane bulges and the lever rises; when the pressure diminishes the membrane collapses and the lever falls. The record, so obtained, gives a much more accurate representation of the actual changes in blood pressure inside the vessels than the Ludwig Kymograph.

**Frank's Manometer**—A further improvement on Hürthle's manometer has been made by Frank who dispenses with the lever. He attaches a SMALL MIRROR to the edge of the rubber membrane and projects a BEAM OF LIGHT on it, the reflected ray being photographed on a MOVING SENSITIVE PLATE. In this way the slightest movement of the membrane and mirror is greatly magnified. The mass and momentum of the apparatus is here reduced to a minimum.

With any of these pieces of apparatus we can measure the blood pressure in an anæsthetized animal and study the effect of various experimental conditions upon it.

**Effect on Blood Pressure of Dividing one or both Vagi Nerves in the Neck**—When one or both vagi are divided in the neck the heart will be freed from the control of the cardio-inhibitory center and will beat faster, consequently the BLOOD PRESSURE WILL RISE.

**Effect on Blood Pressure of Stimulating Peripheral End of Divided Vagus**—Stimulation of the peripheral end of the cut vagus will excite the cardio-inhibitory fibers and so slowing or stoppage of the heart will take place and A FALL IN BLOOD PRESSURE WILL FOLLOW.

**Effect on Blood Pressure of Stimulating Central End of Divided Vagus**—The vagus contains fibers (depressor) running up from the heart excitation of which causes inhibition of the vaso-constrictor center and dilatation of the arterioles with a consequent SLOW FALL IN BLOOD PRESSURE. Other effects may also be produced.

In the rabbit these fibers which reflexly cause a fall of blood pressure and a slowing of the heart are found in a single nerve—a branch of the vagus—called the DEPRESSOR NERVE. In other animals, and in man, they are mixed with the other fibers of the vagus.

**Effect on Blood Pressure of Stimulating Central End of Divided Sciatic Nerve**—Most nerves contain afferent fibers (pressor) which when stimulated excite the vaso-constrictor center reflexly and so RAISE THE BLOOD PRESSURE. This will probably follow stimulation of the central end of the sciatic nerve.

Thus, we see that the blood pressure may be altered by acting on the heart or by acting on the arterioles.

### Blood Pressure in Man

In man the blood pressure cannot be measured, of course, by opening an artery and tying a glass tube into it, so some other device must be resorted to. The apparatus used is called a **Sphygmomanometer** of which there are several forms; the following description refers to the Riva-Rocci pattern.

**The Riva-Rocci Sphygmomanometer** consists of a LEATHER STRAP, about 3 inches wide, which is buckled closely around the upper arm when it is desired to measure the pressure in the BRACHIAL ARTERY. Inside this band, between it and the skin, is a RUBBER BAG which communicates with a MERCURIAL MANOMETER, by means of a rubber tube, and on the same air system is a BICYCLE PUMP by means of which the bag may be inflated. To use the apparatus the physician places his finger on the pulse at the wrist of the subject whose blood pressure is to be taken, and then pumps air into the bag until the pulse is obliterated. He then, by turning a tap, allows air to escape slowly from the system and notes the height of the mercury in the manometer at the moment when the pulse returns which may be determined either by the finger or better by a stethoscope; this will be a measure of the blood pressure in the brachial artery.

The principle is simple. The air pressure in the bag, exerting itself through the skin, closes the artery so that the pulse wave cannot come through. When air is allowed to escape until the pressure inside the artery is just able to open it and let the wave through, the pulse is felt again at the wrist or may be heard with the stethoscope. At that point the pressure in the artery will be practically the same as that in the rubber bag, and the latter is indicated by the height of the mercury in the manometer attached.

This will give the **systolic pressure,** i. e. the pressure in the vessel at the height of the ventricular systole. The pressure in the vessel, at the end of diastole, is much lower and is called the **diastolic pressure** which may also be measured, but for a description of the method one of the larger text-books must be consulted.

The **mean blood pressure** is practically the mean of the systolic and diastolic pressures, and with a rapidly beating heart this is approximately recorded by the Ludwig mercurial manometer.

The normal systolic blood pressure in man (20–25 years) is about 110 mm. of mercury. It increases with age mainly because of loss of elasticity in the arterial walls.

The dangers of a continuous high blood pressure are: 1, that since it is more difficult for the heart to pump the blood against a high than a low pressure that organ may fail, and 2, that the arteries may rupture; this most frequently happens in the brain and so leads to apoplexy.

**Blood Pressure in Veins and Capillaries**—The method of measuring the blood pressure in the veins is the same as that employed for the arteries, except that water is used in the manometer instead of mercury. The pressure in any vein is only from one-tenth to one-twentieth of what it is in the corresponding artery.

**In the capillaries** it is impossible, on account of their size, to introduce a cannula so the pressure is measured indirectly by finding what weight is necessary to blanch the skin, i. e. squeeze all the blood out of the skin capillaries, and from the extent of the area so blanched the pressure is calculated.

## PULSE WAVE

**The Pulse Wave** is caused by the temporary expansion of a blood-vessel due to the sudden injection into it of blood from the heart.

The energy of the heart is expended in two ways—1, in causing an ONWARD MOVEMENT of the blood, and 2, in producing a LATERAL PRESSURE in the arteries. The lateral pressure distends the walls of the arteries and this gradually becomes converted into an onward movement by their elastic recoil.

The pulse wave is usually confined to the arteries and is rarely seen in the capillaries and veins.

**Reason why Pulsation is Confined to Arteries**—If two tubes, each 10 feet long, say, be connected with a rubber ball pump, the one of metal (lead or brass) and rigid, the other of rubber tubing and elastic, and if the distal end of each be constricted with a narrow glass nozzle, when fluid is pumped into the rigid tube the flow will be interrupted or pulsatile, but when pumped through the elastic tube it will be almost continuous. In the case of the rigid tube just as much fluid flows out as is driven in, because water is incompressible, and there is no expansion of the walls; the flow, therefore, must be interrupted since the pumping is interrupted. With the rubber tube it is different; every time fluid is pumped in, the walls expand to accommodate it and then, when the pump ceases to act, the recoil of the elastic wall on the enclosed fluid still propels it forwards, and so keeps up a continuous stream. This latter is the condition in the blood-vessels, and it shows why the pulse is obliterated at the arterioles and does not reach the capillaries. If the nozzle be removed from the rubber tube—a condition resembling dilatation of the arterioles in the body—then the flow is interrupted, because the fluid escapes so easily that there is no pressure exerted on the walls to distend them during the contraction of the pump, and consequently no heaping up of fluid in the system.

The pulse is usually extinguished at the arterioles, 1, because normally these are constricted, and 2, because the arterial walls are

elastic. If the arterioles were dilated or if the vessel walls were rigid then the pulse would not be obliterated at the arterioles; it would be present in the capillaries and even in veins.

The continuous flow in the capillaries permits of the even and steady exchange of material between the blood and the tissues, and it also prevents the capillaries being ruptured by sudden changes in pressure.

**Characters of the Pulse**—The pulse is usually felt in the radial artery at the wrist, first because it is superficial and easily reached, and second because the artery can be readily compressed against the bone which lies behind it.

Many important facts relating to the condition of the heart and circulation can be made out by the trained finger of the physician, such as rate, regularity, force etc., but for the determination of the secondary waves a tracing must be obtained by an instrument known as the sphygmograph.

**Dudgeon's Sphygmograph**—This consists essentially of a small pad or button which is placed on the radial artery at the wrist and which communicates its movements, due to the expansion and contraction of the artery, to a series of levers, the last of which is provided with a writing point by which its oscillations are recorded on a strip of smoked paper moved by clock work. By strapping this apparatus to the wrist a PULSE TRACING OF SPHYGMOGRAM can be obtained.

**Character of Pulse Tracing**—Such a tracing will show, generally, an upstroke or ascending (**anacrotic**) limb, due to the expansion of the artery, and a downstroke or descending (**katacrotic**) limb, due to its retraction. On the descending limb there are two well marked secondary elevations called the **dicrotic** and **predicrotic waves,** D and PD in the diagram, A being termed the **primary** or percussion wave.

**Causes of Waves in Pulse Tracing**—The primary wave A is due to the sudden expansion of the artery by the blood driven into it from the heart, when the aortic semilunar valves open.

**The dicrotic** is a reflected wave from the closed semilunar valves. When the blood tends to rush back into the heart, as the ventricles begin to relax, the aortic semilunar valves give way a little and are then suddenly brought up; this gives rise to a secondary wave reflected forwards from the closed valves.

**The cause of the predicrotic wave** is not so certain. At one time it was believed to be purely instrumental, due to the rebound of the lever as it falls back on the resisting vessel wall, and not to be present at all inside the vessel. It is now believed by many to be a reflected wave like the dicrotic, not from the closed semilunar valves, however, but from points in the arterial system where the

vessels branch. These form a series of promontories projecting into the blood bed and parts of the primary waves, striking these promontories, are reflected backwards, giving rise to the predicrotic wave. The predicrotic wave is best marked when the blood pressure is high.

### Velocity of Pulse Wave and How Measured

The time taken for the pulse wave to travel from the heart to the radial artery at the wrist may be measured by placing one cardiograph on the chest to record the apex beat, and another on the wrist to record the pulse. The two tambour lever points having been arranged on the same vertical line, when the drum revolves the curve produced by the lever connected with the heart will appear in advance of that from the lever connected with the artery. A time tracing is taken underneath, and a vertical line dropped from the point where each curve begins, cutting the time tracing. This will give the time interval between the beginnings of the two curves, that is, the time taken for the pulse wave to travel from the heart to the wrist. Now measure the distance as correctly as possible, along the vessel, from the heart to the wrist and calculate the velocity in feet or meters per second.

The pulse wave reaches the wrist about 1/10th second after it leaves the heart; it takes a little longer to reach the foot, viz.: 1/6 second. Supposing that the distance along the vessel from the heart to the wrist is 3 feet, then the velocity will be 30 feet per second.

See demonstration with long rubber tube to illustrate this method.

## THE BLOOD STREAM

### Circulation in Web of Frog's Foot

If a frog be immobolized with curare and the web of the foot spread out under a microscope, the blood may be seen through the transparent skin, circulating in the arteries, capillaries and veins. The capillaries are so small that the red corpuscles have to go through in single file. In the case of the larger vessels the arteries can be distinguished from the veins by the fact that the former show pulsation while the latter do not. Also, if a part of the field be found where a vessel divides, if it is an artery the direction of flow will be from the larger stem to the branches, if a vein it will be from the branches (tributaries) to the stem.

### Velocity of Blood in Arteries, Capillaries and Veins

The blood everywhere encounters resistance to its movement on account of friction. There is **internal resistance** due to the friction between the particles of a viscous fluid, and **external resistance**

produced by the friction of the blood against the vessel walls; this external resistance is much greater than the internal.

There is a tendency for the blood to adhere to the lining membrane of the vessels so that the external stratum moves very slowly. In the arteries and veins the RED BLOOD CORPUSCLES may be seen moving in the CENTER OF THE STREAM (axial stream) because they are heavier than the WHITE CORPUSCLES and the latter are wedged aside into the PERIPHERAL STREAM.

The velocity of the blood stream in arteries and veins may be measured by an apparatus termed the **hæmodromometer** devised by Chauveau. It consists of a metal tube, the same size as the bloodvessel, let into the side of which is a flange, provided with an index, that moves over a graduated scale.

When this is to be used the artery (or vein) is severed, and the metal tube tied in between the two ends, so that the blood must pass through it. The impact of the moving fluid against the flange, moves the index over the scala, and the number at which this stands will give the velocity of the blood in meters per second. The instrument must be graduated before use by passing through it streams of water of known velocity so that "the angle of deflection may be expressed in terms of absolute velocities."

The velocity is not constant; it varies with the different phases of the heart beat. It is greatest just after the semilunar valves open and allow a fresh inflow of blood from the heart, and gradually diminishes to the end of diastole. The average for the whole cardiac cycle is the MEAN VELOCITY.

**The mean velocity of the blood in the carotid artery** of the horse is about 10 inches per second, and in the internal jugular vein about half as much, viz. 5 inches per second. The velocity of the pulse wave is, as we have seen, 30 feet per second. This is a great contrast. The reason is that the one (pulse) is a pressure wave while the other is the movement of the whole mass of fluid against great resistance.

**The velocity of the blood in the capillaries** is estimated by the microscope to be from 1 to 1½ inches per minute. This is very slow, but the capillaries are so short, that the blood quickly passes through them, nevertheless. In round numbers it may be said that the velocity of the blood in the aorta is one foot per second and in the capillaries one inch per minute.

**Relative Velocities in Arteries, Capillaries, and Veins.**—While the ABSOLUTE VELOCITY will vary with any change in the rate and force of the heart or in the calibre of the arterioles, the RELATIVE VELOCITIES in arteries, capillaries and veins will depend entirely on the width of the bed through which the blood flows, that is, on the united sectional area of the vessels at any level. If the heart

beats faster or more powerfully the blood will move faster in arteries, capillaries and veins, but the relative rate of flow will be the same. The blood stream might be compared with a river (arteries) expanding into a lake (capillaries) and then narrowing down again into an outflow about twice as wide as the inflow river (veins). The flow will be swiftest in the narrow part, slowest in the lake and intermediate in the emerging stream.

If an artery divided into two branches, the sum of their sectional areas will be greater than the sectional area (area of cross section) of the vessel before branching. The arterial system might be compared to a tree, where the sum of the cross sections of all the branches is greater than that of the single trunk.

The blood from the heart flows through a bed which grows wider and wider as it passes from the aorta to the capillaries and narrower and narrower from the capillaries to the large veins. It is estimated that the united sectional area of all the capillaries is 800 times as great as that of the aorta, therefore, the velocity will be 800 times less. The cross section of the large veins (inferior and superior venæ cavæ), as they enter the heart, is about twice that of the aorta at its origin, so that the velocity will be about half what it is in the aorta.

## Circulation Time

By this is meant the time taken by the blood to pass once from the heart, through the vessels, back to the heart again, i. e. to make one complete circulation. In man this is something less than half-a-minuet (23 seconds calculated). The actual time differs in different animals, but in general it appears to take from 26 to 28 heart beats to effect one complete circulation. In man all the blood in the body passes twice through the heart in less than one minute.

## Discovery of the Circulation

It took civilized man several thousand years to discover that the blood movesthrough the heart in a circle. That it actually does so was first proved by Harvey about the year 1616. He made many experiments on himself and on the lower animals of which the following are examples:

He tied a string around the neck of a common grass snake and then beheaded it; the string prevented bleeding. In this cold blooded, decapitated animal the heart continues to beat for a long time. On this snake preparation (no pain could be felt because the brain had been removed) he observed:

1. That when the large veins entering the heart were ligatured the heart and aorta quickly became empty while the veins filled up behind the ligature.

2. In a similar preparation he tied a ligature around the aorta near the heart and then observed that the veins and heart filled up and the aorta beyond the ligature became empty.

3. He opened the aorta and found that the blood spurted out in jets from the end next the heart whenever the ventricles contracted.

4. He opened the vena cava and observed that the blood flowed out steadily, without pulsation, from the end of the vein farthest from the heart.

These experiments showed clearly that the blood flowed from the veins into the heart and out of the heart into the aorta. He stated that the blood passes from the arteries to the veins through pores in the tissues but he was not able to demonstrate the existence of capillaries. These were discovered by Malpighi a few years after Harvey's death.

## THE BLOOD

**The blood** is an internal medium containing nutrient substances on their way TO the tissues, and waste products on their way FROM the tissues to be excreted or removed from the body.

The amount of blood in the body is about 7% of the body weight, or about 5 liters (10 pints) in a man of average size. The specific gravity varies from 1055 to 1060; the color is red when seen in mass but yellow in thin layers; the reaction is slightly alkaline, never acid.

The blood may be regarded as a tissue consisting of cells—the red and white blood corpuscles and the blood-plates, and interstitial substance—blood plasma or liquor sanguinis—in which the cells are suspended.

### Red Blood Corpuscles or Erythrocytes

The size and shape are constant in the same species but different in different species. They are largest in amphibians, such as the frog, and in some of these (amphiuma) they can be seen with the naked eye. In mammals they are smallest in the deer and largest in the elephant. In man they measure about 7 micro-millimeters or 1/3200 inch in diameter. In all mammals, except the camel tribe, they are biconcave discs without a nucleus; in the camel tribe they are non-nucleated but biconvex and ellipsoidal in shape. In all other vertebrates—birds, reptiles, amphibians, fishes—they are ellipsoids, flattened but with a central elevation on both sides and nucleated.

**Number**—In man they number about 5,000,000 per cubic millimeter of blood (men 5,000,000 and women 4,500,000) but in the goat they reach as high as 20,000,000 per cubic mm. Taking the volume of blood in the human body as 5 liters, it is found that the total number of red cells in the body reaches the enormous figure of 25,000,000,000,000.

**Structure**—The red cells form little sacs or vesicles surrounded by a delicate transparent colorless **cell membrane** which is of a fatty nature due to the presence of lecithin, and the contents consist mostly of a colored substance termed **hæmoglobin,** usually written Hb. About 90% of the solids of the red corpuscles and over 14% of the whole blood consists of Hb.

### Hæmoglobin

The hæmoglobin content of the red corpuscles is of great importance. It is probably the most complex substance in the body

and has a molecular weight of over 16,000. Its chemical formula is given as

$$C_{758}\,H_{1203}\,N_{195}\,S_3\,FeO_{218}.$$

It consists of a protein element (globin), which contains all the sulphur, and a pigment (hæmatin), which contains all the iron.

It is easily obtained in the CRYSTALLINE FORM by adding water or ether to blood; the envelopes of the red cells rupture, the Hb escapes and is dissolved in the plasma. On standing it crystallizes out and the crystals falling to the bottom may be examined under the microscope. In most animals, and in man, they are rhombic plates, but in the guinea pig, squirrel and hamster they assume peculiar forms. According to recent work by Reichert and Brown it would appear that the Hb crystals are specific for each animal species, and might thus be used as a character in zoological classification.

THE CHIEF PROPERTY OF Hb IS ITS POWER OF COMBINING WITH OXYGEN; it links on oxygen from the air in the lungs and then gives it up to the tissues.

**Oxyhæmoglobin** ($HbO_2$) is the name applied to the loose chemical compound formed between the Hb and oxygen. It is this that gives the scarlet color to the blood. This respiratory oxygen can be removed from the $HbO_2$ by adding to it certain reducing agents, such as ammonium sulphide or Stoke's solution, and then it becomes **reduced hæmoglobin.** Both forms, $HbO_2$ and Hb, exist in the blood; there is more oxyhæmoglobin in arterial blood and more reduced hæmoglobin in venous blood. It is only in animals dying of suffocation that all the Hb is reduced.

**Experiment to show change in Color of Blood associated with $HbO_2$ and Reduced Hb.**—Place some defibrinated blood in a white porcelain dish and pass through it a stream of oxygen or ordinary air; it will quickly assume a bright scarlet color due to the presence of $HbO_2$.

Take half a test-tube-full of blood and add to it one-quarter its volume of AMMONIUM SULPHIDE solution; in a few minutes it will turn a dark brown color. Pour some of the blood treated with oxygen into another test-tube and compare the two.

**Carbon Monoxide Hæmoglobin (HbCO)**—Other gases besides oxygen form compounds with Hb and of these the most important is CARBON MONOXIDE (CO). When a stream of ordinary coal gas (which contains large quantities of CO) is sent through blood, or a solution of hæmoglobin, the latter quickly assumes a characteristic cherry-red color due to the formation of this compound HbCO. This is a much more stable substance than $HbO_2$; the oxygen cannot turn out the CO and so the Hb ceases to be a carrier of oxygen from the lungs to the tissues. In consequence of this

the tissues are deprived of oxygen and quickly die of suffocation. This explains the poisonous character of coal or illuminating gas, or of CO from any other source.

**Nitric oxide** (NO) forms a compound with Hb (HbNO) which is more stable even than HbCO and which, if inhaled, will cause death in the same way as CO, but this gas is never met with outside of the chemist's laboratory.

In the tissues of the body the protein part of the Hb molecule is believed to have the power of linking on $CO_2$ to form $HbCO_2$ which is dissociated in the lungs. Hb thus acts as a carrier of $CO_2$ from the tissues to the lungs as well as of $O_2$ from the lungs to the tissues.

### Hæmolysis

In various ways the red cells may be destroyed, and then the hæmoglobin escapes and is dissolved in the plasma, in which condition it has not the same power of combining with oxygen. This escape of Hb from the corpuscle is known as **hæmolysis** and the agents which brings it about are termed **hæmolysins** or hæmolytic agents.

The following are examples of hæmolysins—water, ether, chloroform, blood serum from an animal of different species, and many others. The blood serum of a rabbit, for example, injected into the human subject, or into a cat or a dog, will rapidly destroy the red corpuscles of the latter.

These hæmolytic agents act in different ways. WATER added to blood dilutes the plasma and by a process of osmosis the RED CORPUSCLES swell up and ultimately RUPTURE. The blood is then said to be LAKED.

ETHER AND CHLOROFORM DISSOLVE THE CELL MEMBRANE, which is largely composed of the fat-like substance LECITHIN, and so the contents escape.

The nature of the action in the case of a foreign serum is not understood.

Ordinarily blood, even in thin layers, is opaque, but when it is laked, i. e. when the red corpuscles are destroyed, it becomes darker in color by reflected light and more or less transparent by transmitted light. The reason for this is as follows: The blood corpuscles are solid bodies SUSPENDED in a fluid, and reflect a large proportion of the rays of light which fall upon them, so that when a vessel containing blood is held up between the observer and the light little or none gets through; it is opaque. If the corpuscles are dissolved and disappear, however, little or no light is reflected and much gets through so that it appears darker by reflected light and transparent by transmitted light. If the shape of the corpuscles is altered, as can be effected by the addition of a strong solution of

sodium chloride, so that they reflect more light (they are said to be crenated), the color, by reflected light becomes much brighter.

To demonstrate this take two test tubes and place an inch of blood in each, then to the one add an equal quantity of water and to the other an equal amount of sodium chloride, saturated solution, and compare the colors by reflected and by transmitted light.

### Spectroscope Applied to the Examination of Blood Pigments

When a beam of white light from the sun is passed through a glass prism it is spread out into a colored band—red, orange, yellow, green, blue, indigo, violet—and this is called a **spectrum.** The solar spectrum is interrupted by a number of dark lines which cross it vertically; these are called **Frauenhofer's lines** and are caused by incandescent metallic vapors in the sun's atmosphere. They are perfectly constant in position and serve as a natural scale for the spectrum. They are named after the letters of the alphabet, A, B, C, D, E, etc., the D line in the yellow being especially prominent.

If the beam of light, before falling on the glass prism, be passed through a dilute solution of **oxyhæmoglobin** two dark absorption bands will be seen in the spectrum between the D and E lines. This is characteristic of $HbO_2$ and is used as a test for the same. If now the $HbO_2$ is reduced, by adding to it some ammonium sulphide, the two bands will disappear and a single band, much broader, but still between the D and E lines, will take their place; this is the characteristic spectrum of **reduced Hb.**

**The spectrum of HbCO** also shows two bands and is very similar to that of $HbO_2$, but these two substances can be readily distinguished, with the spectroscope, by the fact that $HbO_2$ can be reduced by ammonium sulphide to show a single band while HbCO cannot be so changed.

Many other pigments, derivatives of Hb, give characteristic spectra.

### Origin and Fate of Red Blood Corpuscles

In the adult the RED CELLS are all believed to be produced in the BONE MARROW normally. In the marrow many nucleated red cells are found but the nuclei are lost before the cells are sent out into the circulation, ordinarily. After severe hæmorrhage, however, when the red cells are greatly in demand in the vessels, nucleated reds are often found in the circulating blood, having been forced out prematurely. They subsequently lose their nuclei in the blood stream.

In the EMBRYO AND FOETUS they are also formed in other tissues, particularly the liver and spleen.

The red corpuscle, in the blood stream, in mammals, is a cell which has lost its nucleus and so probably has only a short existence, but just where it breaks down and disappears is a disputed question. It has been supposed that the liver, spleen, and lymph glands are blood destroying organs but at present most physiologists hold to the belief that they simply go to pieces—die of old age so to speak—in the blood stream. It has been estimated that, on the average, the red corpuscles do not live more than ten days. Large numbers are probably destroyed daily. When they break down the Hb which escapes is seized by the liver and there manufactured into bile pigment.

**Effect of Altitude on Number of Red Blood Corpuscles**—The red cells increase markedly in high altitudes. While the normal number at sea level is in the neighborhood of 5,000,000 per cmm., a short stay at an elevation of 12,000 feet may raise it to 8,000,000 or over. The explanation of this increase given is as follows: At high levels the barometric pressure is low and the amount of oxygen in the air inhaled at each inspiration, is greatly reduced, consequently each red corpuscle that comes to the lungs cannot get a full charge and the tissues suffer from lack of oxygen. This condition might be remedied in two ways: 1. The heart might beat faster or more powerfully so that each carrier (red corpuscle) might make the journey between the tissues and the lungs more quickly; or 2, the number of carriers might be increased. It is the latter method that is adopted by the body. In what way this lack of oxygen stimulates the bone marrow to produce more red cells is not understood.

### Anæmia

The blood, like other tissues, is liable to be diseased and here the number of red cells may be greatly altered.

**In ordinary or primary anæmia,** usually called **chlorosis,** the red corpuscles are only slightly below the normal in number but the amount of Hb in each is greatly reduced; it may be only 40% of what it ought to be. This condition is not uncommon in girls in their "teens," but it is rarely seen in boys or men. The cause appears to lie in the bone marrow which is not able to produce a sufficient quantity of Hb. The treatment is very simple and consists in living in the open air, as much as possible, but particularly in taking iron, in some form, as a medicine. Iron is an important element in the molecule of hæmoglobin and this appears to be all that is required here.

**Pernicious Anæmia**—There is another type of anæmia, much more serious than chlorosis, and that is PERNICIOUS ANÆMIA. Here the red cells may be down to 1,000,000 or even 200,000 per

cmm. although each cell may contain the normal amount of Hb. The cause of this condition is not certain. It is nearly always fatal.

### White Blood Corpuscles

There are many varieties of the white blood corpuscles. They are subdivided according to size and shape of nucleus and the character of the granules found in their protoplasm. They fall into two main groups, the **lymphocytes** and the **leucocytes.** Some are small, scarcely bigger than the red cell, and others are very large. Most of the leucocytes show amœboid movement and act as **phagocytes.**

The normal number of white corpuscles is from 5,000 to 7,000 per cmm., but this varies from time to time much more than in the case of the red cells.

**Functions of White Blood Corpuscles**—Without going into detail, the functions of the white corpuscles are believed to be the following:

1. They are **phagocytic,** that is, they attempt to destroy all foreign bodies found in the blood or tissues, especially pathogenic (disease producing) organisms, by absorbing and digesting them. They form the main defence of the body against the invasion of harmful micro-organisms. All so-called infectious diseases such as diphtheria, typhoid fever, tuberculosis, etc., are caused by the entrance of disease germs, microbes or micro-organisms into the body and one important function of the leucocyte is to protect the body from these.

2. They form **antitoxins.** When disease germs settle down in the tissues they produce toxins or poisons, and to counteract the effects of these the leucocytes produce antitoxins, i. e. substances which neutralize the toxins.

3. They take part in the process of **blood coagulation** in a way that will be explained later.

4. They are said to **absorb fats** and to some extent **proteins** from the **intestinal tract** and carry them into the lacteals or intestinal lymphatics, whence they reach the blood stream through the **thoracic duct.**

### Blood Plates

These are circular or ellipsoidal bodies of small size—less than the red cells. Little is known regarding their structure because they disintegrate very rapidly when the blood is shed and a special technique is required for their examination.

They number about 300,000 per cubic millimeter. Like the leucocytes they are believed to be concerned in the **clotting of blood;** in the process of disintegration thrombin or fibrin ferment is set free which acts on the fibrinogen of the plasma and trans-

forms it into fibrin, the essential part of a blood clot. In the peculiar condition of **hæmophilia,** where the blood does not clot at all or clots very slowly, the blood plates are found to be greatly reduced in number. This occurs in men almost exclusively, very rarely in women, yet it is always inherited through the mother. Persons suffering from this disease are called "bleeders" or hæmophilics. The slightest wound will continue to bleed for days and may prove fatal. No surgeon will operate on such people.

## BLOOD PLASMA

The blood plasma is the fluid part of the blood in which the corpuscles are suspended. It contains a great variety of substances in solution, since it carries the food material to the tissues and, at the same time, conveys the waste products away from them. (See composition of plasma on board).

About 90% is water. The PROTEINS are serum albumin, serum globulin, nucleo-protein and **fibrinogen.** The last is present in only small amount but it is a very important constituent.

Under the heading "extractives" a great variety of substances are included. Any organic substance, other than proteins, which may be dissolved out of the dried blood residue by water, alcohol or ether is called an extractive. **Amino acids,** although present in small quantity at any one time, form one of the most important groups. The carbohydrate is present in the form of **glucose.**

Less than 1% (0.85%) of the blood plasma consists of inorganic salts, the chief of which is **sodium chloride.**

In addition to the above, a large number of substances, of unknown composition, which cannot be classified, exist in the blood, in traces, such as enzymes, hormones, immune bodies, opsonins, etc.

The composition of the blood is very constant. The tissues and cells of the body are very sensitive to changes in its composition and strive to keep it constant.

### Coagulation of Blood

Blood when it escapes from a blood-vessel becomes a solid jelly; in other words it clots or **coagulates.** In man this change takes place in from 2 to 4 minutes, in the horse not for about 10 minutes. It is very important that the blood should clot, since this serves to plug the blood-vessels and spontaneously arrest hæmorrhage.

This blood clot, when examined, is found to consist of fibrin threads with the corpuscles entangled. On standing it contracts slowly and a clear fluid, called blood serum, is squeezed out.

When the blood is caught in a beaker and vigorously stirred with a stick or a bunch of twigs the fibrin formed collects on the stirrer

and can be removed, leaving behind the serum and corpuscles; this is termed **defibrinated** or "whipped" blood. When the fibrin is washed free from any corpuscles which may have adhered to it, it is found to consist of a mass of fine elastic threads. This is the essential part of the clot the corpuscles being merely entangled in the fibrin meshwork. How is the fibrin formed?

**Formation of Fibrin**—The fibrin is formed from the **fibrinogen** of the plasma. As we have seen, one of the protein constituents of the plasma is fibrinogen, which is present in solution, and when the blood is shed, this soluble fibrinogen is transformed into insoluble fibrin. This change is brought about by an enzyme or ferment termed fibrin ferment or **thrombin** which does not exist in the blood-vessels as such but rather as an inactive substance termed **pro-thrombin** or **thrombogen.** How is the thrombin formed?

**Formation of Thrombin**—The formation of thrombin is a complicated process. The blood plates and, to some extent the leucocytes, contain prothrombin and when these break down this substance is set free. In the red and white corpuscles, and also in the other tissues of the body such as muscle, there is another ferment termed **thrombokinase;** this, in the presence of soluble calcium salts, acts upon the liberated prothrombin and transforms it into thrombin which then, in turn, acts on the fibrinogen of the plasma and changes it, in some way, to insoluble fibrin. In tabular form the changes which take place may be represented as follows:

Tissue Cells including Blood Corpuscles = **Thrombokinase.**

Thrombokinase + Calcium + Prothrombin = **Thrombin.**

Thrombin + Fibrinogen = **Fibrin.**

Fibrin + R. and W. Corpuscles caught in Meshes = **Clot.**

The above is one of several theories to explain the changes that take place in the spontaneous coagulation of the blood.

**Reason why Clotting does not take place in Vessels**—Any condition, such as contact with a foreign body, which will rapidly break down the blood plates and white corpuscles will hasten the clotting of blood. In the living vessels all the cellular elements are constantly undergoing disintegration but not EN MASSE, as is the case when the blood comes into contact with a foreign body, and not a sufficient quantity of prothrombin and thrombokinase is set free at any one time to have an effect. If a needle be thrust through the vessel wall, into the blood stream, clotting takes place, however, around the needle very rapidly. Injury to the vessel walls also induces clotting, because the damaged tissue really plays the part of a foreign body which rapidly breaks down the blood plates and white cells.

**Calcium in Solution Necessary for Clotting of Blood**—The addition of a small quantity of POTASSIUM OXALATE to the blood will

prevent clotting. The reason is that the calcium oxalate which is formed is insoluble and so all the calcium in the blood is taken out of solution. Since soluble calcium is essential, as well as prothrombin and thrombokinase, to the formation of thrombin, none of the latter is produced and clotting does not take place.

Clotting is RETARDED OR PREVENTED by a LOW TEMPERATURE, by LEECH EXTRACT, and by contact with OIL, etc. The leech feeds on the blood of other animals and the glands of his mouth contain a substance termed HIRUDIN which prevents the clotting of blood, so that it may be more easily digested. If a trace of this substance be injected into the vessels of a living animal the blood will not clot.

**Blood Plates Related to Clotting of Blood**—In birds the blood plates are few and the blood is long in clotting.

In "bleeders" or hæmophilics the blood plates are also few in number and clotting takes place very slowly or not at all.

### Transfusion of Blood

By this is meant the passage of blood from one individual into another. It is sometimes practised in cases of severe hæmorrhage, in CO poisoning, and in pernicious anæmia.

There are two DANGERS associated with the operation. 1. INTRAVASCULAR CLOTTING may take place. If the peripheral end of a vein of the "donor" be connected, by means of a glass tube, with the central end of the vein of the "recipient" the blood, in flowing through the tube, will come into contact with a foreign body (wall of tube) and this may induce clotting in the vessels of the recipient. The surgeon, if sufficiently skillful, however, may overcome this danger by stitching the two veins together so that the blood may flow directly from the one vessel into the other without coming in contact with any foreign body. 2. The DONOR and the RECIPIENT must belong to the SAME SPECIES because of the hæmolytic action which the serum of one animal has on the red corpuscles of another not of the same species. 3. Aseptic defibrinated blood may be used.

In cases of severe hæmorrhage it is just as effective to inject normal saline (0.9% sodium chloride) into the vein as whole blood, since the danger here comes from the fall in blood pressure, not from the loss of blood corpuscles, and no risk is connected with the procedure.

## RESPIRATION

Respiraton consists essentially of an interchange of Oxygen and $CO_2$ between the organism and its surrounding medium. All living things require oxygen and all give off $CO_2$. In the unicellular organism there is no special respiratory apparatus, since this exchange takes place through the entire surface of the body. In all the higher animals a special apparatus is developed to bring the oxygen from the outside environment to the inner tissues and the $CO_2$ from the tissues to the outside, the blood acting as the medium.

In fishes the gills fulfill the same functions as the lungs in air breathing animals. Essentially a gill or a lung consists of a thin MEMBRANE one surface of which is exposed to the medium containing the oxygen—water or air— and the other to the blood. It is through this membrane that the interchange takes place. The same exchange occurs in the tissues but in the opposite direction.

By the term **"inner respiration"** is meant the exchange of gases between the blood and the tissues, and by **"outer respiration"** the exchange between the blood and the air in the lungs (or water in the gills). The inner or true respiration takes place in the tissues.

## THE RESPIRATORY APPARATUS

The respiratory apparatus in man consists of the RESPIRATORY PASSAGES (including the mouth, nose and throat, the larynx, trachea, and extrapulmonary bronchi), LUNGS and MUSCLES OF RESPIRATION (diaphragm and intercostals).

**The Trachea or Windpipe** in the human subject is from 4 to 4½ inches long and from ¾ to 1 inch in diameter. It is formed of a series of cartilaginous rings, defective behind where they lie against the gullet, and is lined by ciliated epithelium. Numerous glands pour their secretions, containing a large amount of mucus, into the trachea and this helps to entangle any dust particles which may be inhaled. The cilia lash upwards and expel the dust laden mucus, through the glottis, into the mouth.

The trachea divides into two **extra pulmonary bronchi,** right and left, the structure of which is practically the same as that of the trachea. In the smaller bronchi (intrapulmonary) the cartilaginous rings are entirely absent; they consist essentially of connective tissue with non-striped muscle fibers, arranged circularly, and are lined by ciliated epithelium.

**The Lungs,** right and left, together with the heart, practically fill the chest cavity. Each lung is partially divided into LOBES of which the right lung has three and the left two.

Each lung consists essentially of a large number of air saccules (alveoli), with a dense network of capillaries in their walls, through which an interchange of gases can take place. The bronchi are continued down from the trachea and when they enter the lung are termed **intrapulmonary bronchi;** they divide and subdivide just like the branches of a tree, getting smaller and smaller until finally each of them terminates in a grape-like cluster of small hollow cavities called **alveoli** or air-cells. The smallest bronchi are termed **bronchioles** just as the smallest arteries, as we have seen, are known as arterioles. The wall of the air cell consists of connective tissue, mostly of the **elastic** variety; this is lined by **endothelium** with a dense network of **capillaries** underneath. All that intervenes between the air and the blood are two layers of endothelium, one lining the capillaries, the other the alveoli. The total extent of the inside of the lung, if it were spread out on a flat surface, is equal to about 90 square meters or nearly 1000 square feet.

**Blood-vessels of Lung**—There are two sets of blood-vessels in the lung just as there are in the heart—the **pulmonary** and the **bronchial.** The pulmonary arteries, capillaries and veins carry the blood through the lungs, from the right side of the heart to the left, for aeration; the bronchial vessels, very much smaller than the pulmonary, carry blood to nourish the lung tissue itself, and correspond to the coronary or nutrient system of the heart.

**Relation of Lung to Chest Wall**—The chest wall is lined by a serous membrane, the **pleura,** which is reflected on to the surface of the lungs. There are two layers, therefore, termed the **parietal** (lining chest wall) and **visceral** (lining lungs) layers of the pleura. No actual space exists in health between these two layers, only a potential space. The one layer rubs on the other, and to diminish friction, the pleura is covered by a single layer of endothelium. When the pleura is the seat of inflammation (pleurisy) the surfaces may be roughened and then "friction sounds" are heard by the physician.

If in the process of inflammation fluid is effused (poured out) between the two layers of the pleura it will cause some collapse of the lung; this condition is known as **Hydrothorax** (water in thorax).

If an opening be made in the chest wall, or in the lung, air will enter the pleural space and the lung will collapse; this is known as **Pneumothorax** (air in thorax). Air may enter through the visceral pleura in phthisis pulmonalis and lead to the same result.

## MECHANISM OF RESPIRATION

By this is meant the mechanical means by which air is drawn into and expelled from the lungs in the alternate phases of inspiration and expiration.

Normally the lungs always fill the chest cavity. Any increase in the size of the chest cavity causes an increase in the size of the lungs therefore air is drawn in through the trachea and this forms the act of **inspiration.** Any diminution in the size of the chest cavity is followed by a reduction in the volume of the lungs; air is expelled and this forms the act of **expiration.**

These changes in the size of the chest cavity are brought about as follows:

**In Ordinary Inspiration** (quiet breathing) the vertical diameter of the chest is increased by the contraction of the **diaphragm.** This sheet of muscle, between the thoracic and abdominal cavities, arches upwards into the thorax and when it contracts it tends to become flattened, thus increasing the **vertical diameter** of the cavity.

The lateral (side to side) and antero-posterior (back to front) diameters are increased by the elevation and rotation of the ribs. The ribs slope downwards and forwards from the spinal column. They articulate with the bodies of the thoracic vertebræ behind, and in front they are connected with the sternum, through the costal cartilages. Between the adjacent costal arches there are two thin sheets of muscle—the **external** and **internal intercostal muscles**—and when these contract the ribs are raised. The posterior ends are fixed so that each rib describes the arc of a circle, and since it slopes downwards, its anterior or sternal end will move forwards; this increases the **antero-posterior diameter** of the chest.

Not only do the contracting intercostal muscles compel the ribs to make this movement, but they (the ribs) are also rotated around an axis passing through the head of the rib and its junction with the sternum, and in this way the **lateral diameter** of the chest is increased.

The chest cavity is therefore enlarged in all dimensions, the lungs follow and air rushes in = **inspiration.** (Illustrate with lungs in glass jar the bottom of which consists of a thick rubber membrane to represent the diaphragm).

The chief muscles of ordinary inspiration are the diaphragm and intercostals, although a few others not mentioned here play a minor part.

**Ordinary Expiration** is non-muscular. It is brought about by four factors, viz.:

1. The Elasticity of the Lung. It is very important to remember that the lungs are elastic. They are always stretched, and tending to collapse, but are unable to do so because they

cannot separate the two layers of the pleura. In the so-called pleural cavity a vacuum exists, and as soon as air is admitted, making the pressure on that aspect of the lung equal to the atmospheric pressure exerted through the trachea, the lung collapses BECAUSE OF ITS ELASTICITY.

2. WEIGHT OF CHEST WALL. The ribs, and all the structures attached to them, are elevated in inspiration and when the intercostal muscles relax they fall in virtue of gravity.

3. UNTWISTING OF COSTAL CARTILAGES. The costal cartilages, attaching the ribs to the sternum, are twisted by the rotatory movement of the ribs; they tend to untwist and this helps to bring the ribs back to the position of expiration.

4. ELASTICITY OF ABDOMINAL WALLS. In inspiration the descent of the diaphragm, which is active, exerts pressure against the abdominal viscera and pushes out the walls of the abdomen putting these under a certain amount of tension. When the diaphragm relaxes, at the end of inspiration, the elasticity of the abdominal walls exerts itself against the abdominal contents and pushes these up against the diaphragm, so that its ascent, by which the vertical diameter of the chest is diminished, is passive. The muscular part of the diaphragm has no power to arch upwards into the thorax if it is not pushed from below.

**Respiratory Movements in Male and Female**—Respiration in the MALE is carried on mainly by the DIAPHRAGM; in the European and American FEMALE mainly by the RIBS. In the CHILD the movements are chiefly DIAPHRAGMATIC in both sexes. In Indian and Chinese women, who have never worn tight dress, the movements do not differ from those of the child and of men, and this shows that the costal type is due to the vicious habit of wearing tight corsets which prevent the normal movements of the abdominal walls.

In dyspnœa or threatened suffocation the breathing is decidedly costal.

**A graphic record of the respiratory movements** may be obtained by the use of an instrument termed the **Stethograph** or **Pneumograph.** The simplest form consists of a wide rubber tube, containing a spiral spring, one end of the tube being closed and the other attached to a tambour, provided with a lever, writing on a revolving drum. The rubber tube is strapped around the chest with an inextensible chain.

During inspiration air is drawn out of the tambour into the tube and the lever falls; during expiration the air re-enters the tambour and the lever rises. If a time tracing be taken underneath, the relative duration of the different phases may be determined. The rhythm is, inspiration—expiration—pause, and the relative dura-

tion of each phase is 3:4:3. If the pause be taken as a slow expiration, which in reality it is, then the ratio will be inspiration 3: expiration 7.

**The respiratory sounds** are caused by the air entering and leaving the lungs. The character of these is of great importance to the physician as a guide to the condition of the lungs.

**Innervation of Diaphragm and Intercostal Muscles**—The diaphragm is supplied by the two PHRENIC NERVES, right and left, and the intercostal muscles by eleven pairs of INTERCOSTAL NERVES from the thoracic region of the spinal cord. The phrenic nerve on each side arises from the 4th and 5th cervical spinal segments so that section of the spinal cord above this level stops the respiratory movements completely and is, of course, fatal. If the cord be injured below the 5th cervical segment, although the intercostal muscles are cut off, respiration by the diaphragm can still be carried on.

## RESPIRATORY CENTER

The rhythmical movements of respiration require the harmonious action of a number of different muscles, and where this is the case, these muscles must be presided over by a co-ordinating center in the nervous system.

**The respiratory center** is situated in the medulla oblongata. It is bilateral (half on each side) the two halves being connected across the middle line by nerve fibers, so that normally the two sides act together. Injury to this part of the brain paralyzes the respiratory center and causes instant death.

The activity of the respiratory center is REGULATED MAINLY BY THE AMOUNT OF $CO_2$ IN THE BLOOD going to it. Every condition which leads to an accumulation of $CO_2$ in the blood causes an increase in the rate and depth of respiration, e. g. muscular exercise such as running, hill-climbing, etc. The $CO_2$ when it reaches a certain level, excites the cells which form the respiratory center; these send impulses down the spinal cord and out into the phrenic and intercostal nerves, causing the diaphragm and intercostal muscles to contract, and so inspiration is brought about. This removes $CO_2$ so that its level in the blood falls below the exciting point; impulses no longer reaching the muscles in question, they relax and expiration follows.

Diminution of oxygen in the blood acts to some extent as a stimulus to the respiratory center, but this is not such an important factor as the accumulation of $CO_2$.

**Reflex and Central Stimulation of Respiratory Center**—In addition to the effect of $CO_2$ in the blood, the respiratory center is also acted on by impulses reaching it through the peripheral nerves, and by impulses coming down to it from the higher brain centers.

Cold water, for example, applied to the skin of the abdomen or chest produces deep inspiration, due to the reflex stimulation of the respiratory center. Emotion may cause either sobbing or laughing, both of which are modified forms of respiration, by excitations reaching the respiratory center from above.

Coughing, sneezing, yawning, sighing, hiccup are all examples of modified respiration, and are all produced by stimulation of the respiratory center, either reflexly or from the higher brain centers.

A peculiar form of respiration known as **Cheyne-Stokes breathing** is sometimes present in disease. The patient ceases to breathe for a time; the respirations then begin; they are feeble at first, but gradually increase in depth, until a maximum is reached, when they die away again and then cease altogether. After a pause, the same succession follows again. In these cases the respiratory center is less excitable than usual, and it requires a greater accumulation of $CO_2$ to start it than is ordinarily sufficient. Once it wakes up, however, it continues until the excess of $CO_2$ is swept away, and then it goes to sleep again, so to speak.

**Vagus Control of Respiration**—The respiratory rate and depth are controlled, to a large extent, by impulses from the lungs themselves which reach the respiratory center through the vagi nerves—an example of peripheral reflex stimulation.

If one VAGUS NERVE IN THE NECK IS CUT, in an anæsthetized animal, the RESPIRATORY RATE IS DIMINISHED BUT THE DEPTH IS INCREASED; if both are cut the effect is greater still. Two sets of afferent nerve fibers are believed to exist in the vagus, carrying impulses from the lungs to the respiratory center; stimulation of the one excites the center and brings about inspiration, stimulation of the other inhibits the center, checking inspiration, and leading to expiration. The nerve terminations of these fibers end in the walls of the alveoli; one set is excited by the collapse of the walls and the other by their stretching. At the end of expiration the collapse of the lungs stimulates the inspiratory fibers and starts inspiration sooner than would be the case if the $CO_2$ in the blood were alone responsible; similarly, at the end of inspiration the inhibitory fibers are excited by the expansion of the lungs and this checks inspiration. However, when these influences from the lungs are entirely cut off, respiration does not come to a standstill; it is regulated all the time by the $CO_2$ in the blood but the rhythm becomes slower and deeper.

The respiratory center is under the control of the will, to a considerable extent. A person can voluntarily accelerate his respiration or stop it altogether but the latter only for a short time; at the end of about one minute, the desire for air becomes so strong, that voluntary inhibition is ineffective and respiration is resumed.

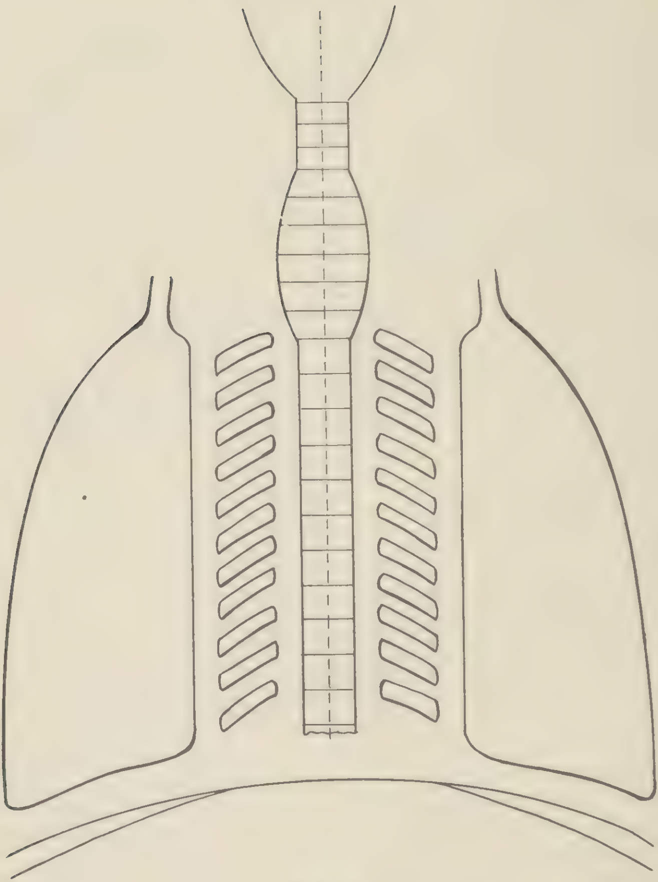


Fig. 8

### Apnœa, Eupnœa, Hyperpnœa, Dyspnœa, Asphyxia

By the term APNŒA is meant no breathing, or rather no desire to breathe. If a person breathe rapidly and deeply for half a minute and then stop, for the next twenty seconds or so he has no desire to breathe, that is, apnœa. This is because the $CO_2$ of the blood has, to a large extent, been swept away and got rid of, and until it accumulates again to the exciting point, inspiration does not take place.

The term EUPNŒA means normal breathing; HYPERPNŒA exaggerated breathing; DYSPNŒA labored or distressful breathing, and ASPHYXIA suffocation from want of air.

## BLOOD GASES

There are THREE GASES present in the blood—OXYGEN, NITROGEN and $CO_2$; all leave it in a vacuum. All the nitrogen is held in solution; the oxygen and $CO_2$ partly in solution and partly in chemical combination.

By means of a complicated piece of apparatus known as a BLOOD GAS PUMP a quantity of blood may be drawn into a vacuum and the mixture of gases which escapes or boils off from it collected and analyzed. If 100 c.c. of blood be treated in the way described it will yield about 60 c.c. of gas, and if this be analyzed its composition by volume will be about as follows:

| Blood | O | $CO_2$ | N | |
|---|---|---|---|---|
| Arterial | 20 | 38 | 2 | c.c. |
| Venous | 12 | 46 | 2 | c.c. |

The oxygen comes almost entirely from the red corpuscles where it exists in loose combination with hæmoglobin as $HbO_2$. It is so loosely combined that it dissociates in vacuo.

The $CO_2$ is contained both in the corpuscles and in the plasma, but mostly in the latter, where it exists as sodium bicarbonate and in organic combination with the proteins of the plasma. Some is present in the red cells as $HbCO_2$. In vacuo these substances dissociate and $CO_2$ is given off, e. g. $2NaHCO_3$ changes to $Na_2CO_3$ setting free water and $CO_2$.

Some oxygen, some $CO_2$ and all the nitrogen exist in the plasma in solution just as they would in water.

**Exchange of Gases between Blood and Air in Lungs and between Blood and Tissues**—Oxygen is at a higher tension in the air cells of the lungs than in the blood and it therefore diffuses from the

air cells into the blood; $CO_2$ is at a higher tension in the blood than in the air cells and it diffuses from the blood into the air cells. An exchange the reverse of this takes place in the tissues. This is simply a case of the diffusion of gases according to well known physical laws.

### Respiratory or Vital Capacity

This term is applied to the amount of air that can be expelled from the lungs by a forcible expiration after they have been fully distended by a forcible inspiration. This volume may be determined by means of a **spirometer.** This instrument consists of a circular vessel, filled nearly to the top with water, and a graduated cylinder inverted over it and counterbalanced by a weight. By means of a vertical tube, fixed to the bottom of the reservoir, and projecting above the surface of the water, the air expelled from the lungs is collected in the cylinder and the amount read off on a graduated scale.

To measure the so-called vital capacity take as deep a breath as possible, hold the nostrils and then expel as much air as possible. For an individual of average height (5 feet 8 in.) the respiratory capacity should be about 3700 c.c. if the lungs are sound. There is found to be a relationship between the height and the respiratory capacity. According to Hutchinson between 5 and 6 feet every inch of stature should add 8 cubic inches (130 c.c.) to the respiratory capacity.

The air inspired and expired at each ordinary respiration is termed the **tidal air;** it is only about 500 c.c. At the end of an ordinary inspiration 1600 c.c. more can be drawn into the lungs by a forced inspiration; this is called the **complemental air.** Then, at the end of an ordinary expiration, 1600 c.c. more can be expelled from the lungs; this is called the **supplemental air.** There still remains in the lungs, after the most powerful expiration, 1000 c.c.; this is termed the **residual air.** The sum of the complemental, tidal and supplemental air constitutes the respiratory capacity.

### Inspired and Expired Air

The atmospheric air which is inspired is very constant in composition. Every 100 parts by volume of the air inspired contains approximately 79 parts of nitrogen, 20.96 of oxygen and 0.04 of $CO_2$. The expired air gains about 4% of $CO_2$ and loses about the same amount of oxygen. A candle will not burn in air that has passed once into the lungs and is then expired. (Experiment to prove this).

Besides the gain in $CO_2$ and loss of oxygen, expired air differs from that inspired by having added to it heat and moisture. A large quantity of heat is carried away from the body in the expired

air, and this is one important factor in the regulation of the body temperature.

### Effects of Breathing a Vitiated Atmosphere

It is difficult to say what are the causes of the evil effects (headache, general malaise, high temperature, etc.) which follow from breathing the vitiated atmosphere of a badly ventilated and overcrowded room. These might be due, 1, to excess of $CO_2$, 2, to want of oxygen, 3, to the presence of some toxic substance in the expired air.

1. If $CO_2$, prepared in the laboratory, be added to the air of a closed chamber until it contains far more than the most badly ventilated room, little or no discomfort is felt from breathing it. Again, the air of a brewery may contain 10 times as much $CO_2$ as the air of a very poorly ventilated room and yet men may work in such an atmosphere for years and remain in good health.

2. There is less oxygen in the air of a mountain health resort than in the most overcrowded rooms at sea level, and yet the effect is exhilarating rather than otherwise. Thus the oxygen of the air can be reduced far below that found in very badly ventilated rooms and the $CO_2$ raised far above it, without any ill effects. If, of course, the diminution of oxygen or increase of $CO_2$ be very great, death may result from asphyxiation or from $CO_2$ poisoning.

3. Is the cause to be found in some organic poison given off from the lungs? This was answered in the affirmative by Brown-Sequard who believed that he had proved the presence of a toxin in expired air.

**Brown-Sequard's Experiment**—He arranged 5 flasks in series and connected them to each other and to an aspirator by rubber tubing, so that a continuous stream of air might be drawn through. Between the 4th and 5th of the series he inserted a tube containing sulphuric acid, and then into each he placed a mouse. The sulphuric acid, while it would allow $CO_2$ to pass through it unaffected, would decompose and destroy any organic substance.

When he started the experiment the first mouse to show any effect was that in flask No. 4, and in some hours it died. Next followed No. 3 and lastly, No. 2, while the mice in flasks 1 and 5 remained alive and apparently quite well.

He explained these results as follows: If $CO_2$ had been the poison then No. 5 should have died first because it received all the $CO_2$ given off by the four mice in front of it, and the sulphuric acid did not interfere with the passage of this substance, but it did keep back any organic toxin which might be produced in the lungs. This toxin would be received in larger quantity by No. 4 than by any in front of it, hence its early demise, and so on for the others.

Nos. 1 and 5 were inhaling air free from this toxin and consequently were not affected.

There is a FALLACY IN THIS EXPERIMENT which was overlooked by Brown-Sequard, however, and that is this. He proved that the death of Nos. 4, 3 and 2 were due to an organic toxin but he did not prove that that toxin came from the lungs. The mice had been kept in the flasks for several hours, in a warm room, and during this time urine and fæces had accumulated; the toxin or toxins were probably some of the decomposition products of these.

If the moisture present in expired air be condensed, and then injected under the skin of an animal, no evil effect results.

NO TOXIN GIVEN OFF BY THE LUNGS HAS EVER BEEN DEMONSTRATED.

It is now generally believed that the PHYSICAL CONDITION of the air has more to do with the bad effects of poor ventilation than its chemical constituents. It has a high temperature, it is stagnant and saturated with moisture, besides being contaminated with offensive exhalations from the teeth, skin and clothes of persons in the room. Under these conditions the temperature of the body rises until the individual suffers from a mild degree of fever.

## Methods of Applying Artificial Respiration to Persons Apparently Drowned, Electrocuted, etc.

When respiration is suspended, as in persons apparently drowned, or from any other cause such as an overdose of chloroform or ether, **artificial respiration** must be carried on to take the place of the normal movements. Several methods have been employed of which the four given below are the most important.

1. **The Marshall Hall Method**—This consists in placing the subject on his side, rolling him over on to his face, and then back to the original side position. These movements are carried out at the rate of about 15 per minute. The respiratory exchange capable of being effected by this method is not great, and besides, the body is liable to be bruised and injured by the manipulation.

2. **The Sylvester Method**—The patient is laid on his back (supine position), the arms are grasped by the operator below the elbows and pulled upwards above the head to expand the chest and produce inspiration; they are then brought firmly down on the front of the chest so as to expel the air and cause expiration. The disadvantages of this method are (a) That the TONGUE FALLS BACK and closes the entrance to the lungs; it must therefore be held forward by an assistant. (b) No opportunity is given for any water, which may have been drawn into the lungs, to escape. (c) The liver is liable to be ruptured. (d) It requires a good deal of muscular effort on the part of the operator.

3. **In the Howard Method** the subject is laid on his back, and pressure is brought to bear upon the lower part of the chest causing expiration. When this pressure is withdrawn, the ribs, on account of their elasticity, return to their original position leading to inspiration. The disadvantages here are the same as in the Sylvester method except that it is not so hard on the operator.

4. **The Schafer Method** is the latest and the best. "It consists in laying the subject in the prone position (face downwards) preferably on the ground, with a thick folded garment underneath the chest and epigastrium (pit of stomach). The operator puts himself athwart or at the side of the subject facing his head (see diagram) and places his hands on each side over the lower part of the back (lowest ribs). He then slowly throws the weight of his body forward to bear upon his own arms, and thus presses upon the thorax of the subject and forces air out of the lungs. This being effected, he gradually relaxes the pressure by bringing his own body up again to a more erect position, but without moving his hands."—Schafer.

The advantages of the Schafer method over the others are: 1. It produces a greater exchange of air than any of them—much more in fact than takes place in ordinary quiet breathing. 2. The tongue falls forward and does not close the entrance to the lungs. 3. Any water which has been drawn into the lungs has an opportunity to flow out by the mouth. 4. It can be carried on for hours without fatigue. 5. There is little danger of rupturing the liver.

The movements above described should be kept up at the rate of about 15 per minute for one hour before hope is abandoned, unless natural respiration returns earlier, or until rigor mortis has set in.

The most important thing to be remembered is that artificial respiration should be started without an instant's delay.

## DIGESTION

All food substances may be divided into five chemical groups, viz.:—**proteins, carbohydrates, fats, salts** and **water** and the first three of these must be digested in the alimentary canal and prepared for assimilation by the tissues; none of them are ready for use when taken into the body except the inorganic salts and water. This digestion or chemical transformation is carried out by secretions which are poured into the alimentary tract at different levels, the active agents being certain enzymes or ferments which they contain.

### Divisions of Alimentary Canal

| | | |
|---|---|---|
| Mouth | | |
| Pharynx | | |
| Oesophagus or gullet | | |
| Stomach | | |
| Small Intestine | Duodenum, first 10 or 12 inches. | |
| | Jejunum, first 2/5 of remainder. | |
| | Ileum, last 3/5 of remainder. | |
| Large Intestine | Cœcum and Vermiform Appendix. | |
| | Colon | Ascending Colon. |
| | | Hepatic flexure. |
| | | Transverse Colon |
| | | Splenic flexure. |
| | | Descending Colon. |
| | | Sigmoid flexure. |
| | Rectum. | |

The liver and pancreas are important glands that pour their secretions into the small intestine.

## SALIVA

The first secretion which acts on the food is the saliva. (For composition see board). It is poured into the mouth by three pairs of salivary glands—the **parotid,** the **submaxillary** and the **sublingual**—and by numerous small glands lining the mouth cavity termed **buccal glands.**

**Secreting Glands**—At this point a word might be said about the structure and functions of secreting glands in general. They consist of saccular or tubular depressions on a free surface and are lined by a single layer of modified epithelial cells, arranged around a central cavity or lumen. The cells have the power of

Fig. 9

taking from the blood or lymph which bathes them the materials out of which they manufacture the particular substance or substances characteristic of the secretion, and this is poured out onto the surface, through the communicating channel which is termed the duct of the gland. According to their complexity they are classified as simple and compound; we have simple saccular and compound saccular glands, simple tubular and compound tubular glands.

### Salivary Glands

The three paired glands just mentioned—parotid, submaxillary, sublingual—are COMPOUND TUBULO-SACCULAR glands, each provided with a duct. They are contained in a connective tissue CAPSULE and are subdivided into LOBES and LOBULES by SEPTA (strands of connective tissue) which pass in from the capsule.

The gland cells, just like muscle fibers, are supplied with nerves stimulation of which leads to activity of the cells and a pouring out of secretion. **The salivary center** consists of a group of nerve cells situated in the medulla oblongata and from these nerve fibers pass to the glands. The submaxillary gland, for example, receives fibers from the chorda tympani (a branch of the 7th cranial nerve); if this nerve be divided and its peripheral end stimulated, saliva will flow from the duct in great abundance.

All nerve centers are capable of being excited reflexly, and the secretion of saliva normally is a reflex act. The stimulus comes from the sapid substances in the mouth which excite the afferent nerve fibers going to the center. The salivary center in the medulla oblongata is also under the influence of the higher brain centers, as in the case of the heart and blood-vessels, etc., and so the mere thought of food may cause the "mouth to water." Emotion of a different kind, such as fear, may have an inhibitory influence on the secretion of saliva, and cause the mouth to become dry.

In the RESTING STAGE the cells become loaded with GRANULES which are discharged during functional activity.

### Physical and Chemical Characters of Saliva

It is a colorless or opalescent, viscid fluid, slightly alkaline in reaction. Its characteristic constituent is the ferment **ptyalin** which has the power of TRANSFORMING STARCH INTO SUGAR. The nature of this transformation is HYDROLYTIC, that is, the molecule of starch takes up water and splits up into the simpler molecules of DEXTRIN and MALTOSE. Dextrin is an intermediate product; the final product is maltose, a reducing sugar. If a warm solution of starch be taken into the mouth and held there for a minute, at the end of that time all the starch will have disappeared and a **reducing sugar will be present.**

Ptyalin is destroyed by free mineral acid, such as HCl, even in great dilution. It acts most rapidly and most effectively at the body temperature; if heated to 60°C. it is destroyed.

**The functions of saliva** are partly chemical and partly mechanical. Its chemical function is to transform starch into sugar; its mechanical function is to moisten the mouth and gullet and so to assist in speaking, chewing, and swallowing. Its slimy character due to the presence of MUCIN is important in this relation. It also serves to dissolve sapid substances in the food so that they can be tasted. In the carnivora, where there is no carbohydrate in the food, ptyalin is absent from the saliva and it has merely a mechanical function.

## MASTICATION AND DEGLUTITION

**Mastication** or chewing the food is brought about by the biting and grinding action of the teeth. This is assisted by the tongue pressing the food against the hard palate, and also by the cheek muscles which keep pushing the food between the teeth. In the process of mastication the salivary glands are very active, and the saliva secreted is intimately mixed with the comminuted food.

Carnivorous animals bolt their food almost unchewed, while vegetable feeders masticate very thoroughly, especially the ruminants. In these animals—cud-chewers—it is first swallowed hurriedly and then brought up again and chewed thoroughly. This is important in herbivorous animals where there is much starch in the food to be converted into sugar. In man, who is a mixed feeder, it is also important that the food be well chewed.

**Deglutition,** by which the food, after mastication, is transmitted from the mouth to the stomach, is a complicated process. It is brought about by the co-ordinated action of the muscles of the tongue, soft palate, pharynx (throat), larynx and gullet. The particles of masticated food are collected into a bolus which is pushed back into the pharynx by squeezing the tongue against the hard palate or roof of mouth. This is voluntary. As it passes through the pharynx, the glottis and the openings into the nose are closed reflexly to prevent the food entering the lungs or coming out through the nose. From the pharynx it passes into the upper end of the gullet where it is seized by this muscular tube and pushed into the stomach by a peristaltic movement. This is involuntary. If the muscular coördination is disturbed so that the glottis is not closed at the proper time some food particles will enter the trachea and give rise to a fit of coughing.

In man, ordinarily, gravity assists swallowing, but in most other animals, which eat off the ground, swallowing takes place against

gravity. Water and other fluids are shot down through the gullet very quickly.

## DIGESTION IN THE STOMACH

**The stomach** is a saccular dilatation on the alimentary canal for receiving and holding the food until it is sufficiently prepared for being passed on into the small intestine where digestion is completed. It has two openings, the cardiac and the pyloric. The cardiac opening communicates with the gullet or œsophagus, a muscular tube lined by mucous glands through which the food reaches the stomach, and the pyloric opening leads into the duodenum.

### Structure of the Stomach

Externally it is covered by PERITONEUM reflected from the abdominal wall. The peritoneum is a serous membrane similar to the pericardium and pleura, already considered, and is lined by a single layer of ENDOTHELIUM. It extends over the abdominal wall and is reflected over the abdominal viscera as is the pleura over the lungs so that it forms the outer layer of each of them.

Inside the peritoneum is found the MUSCULAR COAT which consists of three layers of non-striped muscle, more or less distinct from each other. In the OUTER LAYER the fibers are arranged LONGITUDINALLY, i. e. from the cardiac to the pyloric openings, in the MIDDLE LAYER CIRCULARLY, and in the INNER LAYER OBLIQUELY. The last is incomplete and unimportant. At the pylorus the circular layer is greatly thickened and the fibers are so arranged as to form a SPHINCTER which closes the opening until the muscle relaxes. A similar arrangement is found at the cardiac opening.

Next to the muscular comes the SUBMUCOUS COAT composed of loose connective tissue. Here are found the larger blood vessels, lymphatics and nerves which supply the muscular coat and the mucous membrane.

THE MUCOUS MEMBRANE forms the inner layer of the stomach wall. It consists of a great number of small glands closely packed together side by side which open on to the surface. They are supported by a small amount of connective tissue and are separated from the submucous coat by a thin layer of non-striped muscle termed the MUSCULARIS MUCOSAE which sends a few strands up between the glands.

The stomach is divided more or less artificially into FOUR REGIONS (see diagram). The CARDIA or cardiac region lies immediately around the cardiac orifice; the FUNDUS is the blind rounded end of the stomach to the left of the cardia; the part between the fundus and a transverse band situated towards the pyloric end forms the body of the stomach, sometimes termed the PREPYLORIC

REGION, and the part between this band and the pylorus is known as the PYLORIC REGION.

**Gastric Glands**—Three varieties of glands are found in the mucous membrane of the stomach—CARDIAC, FUNDIC and PYLORIC GLANDS. The cardiac glands, found in the cardia, are simple tubular glands formed of columnar epithelial cells. The fundic glands, which occupy the mucous membrane of the fundus and most of the prepyloric region, are compound tubular glands two or three tubules opening into a single duct through which the secretion is discharged on the surface. The duct is lined by columnar epithelial cells which secrete mucin while the deeper lying tubules contain two varieties of cells, CENTRAL and PARIETAL. The central cells lie next to the lumen; they are cubical or low columnar epithelial cells and granular as distinguished from those lining the ducts which are clear like all mucin secreting cells. The parietal cells lie between those just mentioned and the walls of the tubule; these are oval or spherical and more distinctly granular than the central cells. They do not form a continuous layer. The pyloric glands, found in the pyloric region, are also of the compound tubular variety. They have long ducts lined with clear columnar cells and the secreting tubules contain cells corresponding to the central cells of the fundic glands and no parietal cells.

The PARIETAL CELLS of the fundic glands are believed to SECRETE THE HCl of the gastric juice and the CENTRAL CELLS of the fundic glands, along with these of the pyloric glands, THE PEPSIN. As in all other secreting glands, during the resting stage granules accumulate in the cells and are discharged during the active stage. These granules do not consist of the ferment pepsin, however, but of a pro-substance which might be called pro-pepsin or pepsinogen and which is not active as a digestive agent until, in the process of secretion, it is transformed into pepsin.

**Blood-vessels and Nerves of the Stomach**—The stomach has a very rich blood supply. When it is empty and inactive the mucous membrane is pale because the arterioles are constricted, but when food enters the stomach these vessels are reflexly dilated, allowing more blood to reach the secreting glands, and the surface becomes very red.

THE SECRETORY NERVE FIBERS which supply the gastric glands reach the stomach through the two vagi nerves, right and left. They come from a group of nerve cells situated in the medulla oblongata which forms the gastric secretory center. Like those nerve centers already studied it is capable of being acted on from the periphery reflexly, and from the higher brain centers in the cerebrum.

## Gastric Juice

The gastric juice or stomach secretion may be obtained free from food by establishing, in an animal (dog for example), A GASTRIC FISTULA, that is an opening into the stomach through the abdominal wall; this may be temporary or permanent. Occasionally this procedure is necessary in the human subject, where the gullet has been permanently closed from swallowing a corrosive poison. In order to prevent the patient from dying of starvation an opening (permanent fistula) must be made in the stomach through which food can be introduced.

The fluid so obtained, is clear, colorless and odorless, with an acid reaction. (For composition see board). Its CHARACTERISTIC CONSTITUENTS ARE THE FERMENT PEPSIN AND FREE HYDROCHLORIC ACID. The latter varies from about 0.2% in man to 0.6% in carnivorous animals such as the cat and dog. More than 99% is water.

The hydrolytic action of the ptyalin of saliva on starch takes place, as we have seen, only in a slightly alkaline or neutral medium. This is stopped at once by free HCl but this does not mean that carbohydrate digestion ceases in the stomach. The food mixed with the alkaline saliva, is only penetrated slowly by the gastric juice and until the center of the mass has been reached some transformation of starch into sugar may still go on. Thus, for 20 or 30 minutes after the food enters the stomach, the digestion of any carbohydrate which may have escaped the action of ptyalin in the mouth may be completed in the stomach. Free HCl DESTROYS the ptyalin so that it can't resume its action in the alkaline secretions of the small intestine.

## Digestive Action of Gastric Juice

Gastric juice acts **mainly on the proteins** of the food and scarcely at all on the fats and carbohydrates. The carnivora have a more powerful gastric secretion than other animals; their diet consists mainly of proteins.

The digestive action of gastric juice can be studied by making a mixture of HCl and pepsin in glass vessels kept at the body temperature. **This artificial gastric juice** transforms coagulable proteins, such as egg albumin, meat or fibrin, first into SOLUBLE GLOBULIN, then into acid METAPROTEIN, then into PRIMARY PROTEOSES, then SECONDARY PROTEOSES and finally PEPTONES. The process is again one of hydrolysis; water is added, and then the complex protein molecule splits up into two simpler molecules, and so on until finally the peptones are reached.

THE PROTEIN SPLITTING PROCEEDS NO FARTHER THAN THE PEPTONE STAGE IN THE STOMACH.

The process of digestion can be studied in the human subject by giving a test meal of bread and meat, etc., and withdrawing the contents for examination at definite intervals by means of the STOMACH TUBE. In this way the digestibility of different varieties of the protein food substances may be investigated. The results are practically the same as those obtained by the method of artificial digestion.

In cases of weakened digestion or prolonged starvation, it is advisable to give PEPTONIZED FOOD, that is, food that has already been artificially digested to the petone stage; or pepsin and HCl in the proper quantities may be given along with the food. The reason for this procedure in cases of starvation, for example, is that the gastric glands are unable to produce any secretion in which case the food would remain in the stomach undigested.

**Action of Gastric Juice on Carbohydrates and Fats**—The digestion of carbohydrates takes place almost entirely in the mouth and small intestine, and of fats in the small intestine. The action of the gastric juice on these two classes of food substances is of little importance.

Cane sugar undergoes inversion into equal molecules of glucose and fructose.

On fats the main action is to dissolve the connective tissue frame work of the groups of fat cells, and also the envelopes of these cells, so that the fat contained in them is set free in the stomach and is ready to be acted on in the small intestine.

Gastric juice has the power to curdle milk and this is due to the presence of a ferment termed RENNIN which is produced by a zymogen which is activated by hydrochloric acid.

## MECHANISM OF GASTRIC SECRETION

**Nervous Factor**—The secretion of the gastric juice is under the control of a **nerve center** just as is the salivary secretion, and the secretory fibers pass to the stomach in the two **vagi nerves.** If an opening is made into the stomach, through which its interior can be inspected, and then if one vagus nerve be divided below the point of origin of the cardiac branches, and the peripheral end stimulated, gastric juice will be poured out by the fundic and pyloric glands, after a latent period of about five minutes.

**The gastric secretory center** in the medulla oblongata is capable of being excited reflexly from the mouth. This was proved by the following experiment first performed by Pawlow: He divided the œsophagus of a dog in the neck and brought the two ends to the surface, stitching them to the skin. At the same time he made a permanent opening (fistula) in the stomach through which he could watch the mucous membrane. When the dog masticated and

swallowed food it never reached the stomach, but escaped to the outside, through the upper œsophageal opening. This Pawlow termed **"Sham-feeding;"** the dog could go on eating for hours and still have an appetite.

It used to be supposed that contact of the food with the gastric mucous membrane was necessary to excite secretion, but Pawlow observed that a COPIOUS FLOW OF GASTRIC JUICE took place WHILE THE FOOD WAS BEING CHEWED in the mouth and as long as the sham-feeding went on this flow continued. In some cases he was able to collect almost 1000 c.c. of pure gastric juice, perfectly free from food, in this way, in a few hours. He then divided both vagi nerves and found that the secretion stopped although the sham-feeding was still continued.

Here the AFFERENT IMPULSES reach the gastric secretory center through the NERVES OF TASTE the exciting agent being the sapid substance in the mouth. This stimulates the center which in turn sends impulses to the gastric glands through the vagi. Interruption of the reflex arc at any point, e. g. by cutting the vagi, will stop the secretion.

**Psychical Secretion**—Pawlow also observed that if the dog were hungry the mere sight of food was enough to cause a flow of gastric juice. In this case the stimulus reached the secretory center in the medulla oblongata from the higher brain centers, and this he called "PSYCHICAL SECRETION."

Pawlow found that in order to produce the reflex secretion the food must be AGREEABLE AND APPETIZING; sand or pebbles placed in the mouth produced no affect at all on gastric secretion.

Similar observations have been made on human beings where it was necessary to establish a permanent opening in the stomach, through the abdominal wall, because of occlusion of the œsophagus, and the results agree with those obtained in the dog. When the food was swallowed it did not enter the stomach but was regurgitated back into the mouth, nevertheless, an abundant secretion took place while mastication was going on.

**Chemical Factor**—The nervous stimulation does not account for all the secretion produced during the digestion of a meal, however. If a permanent fistula be made in the stomach of a dog, and if both vagi be divided so as to cut off completely all nervous influence, when meat is introduced into the stomach, through the opening, after an interval of some minutes, gastric juice will begin to flow. Mechanical stimulation of the mucous membrane, such as tickling it with a feather or the introduction of sand, will not produce any flow. If bread or starch or egg albumen be used, instead of meat, no secretion will result. There must, therefore, be some substance in the meat which has the power to excite the gastric glands that is not found in bread, etc. If partially digested

bread be introduced into the stomach secretion does follow, however, so it would appear that the exciting substance is produced in the early stages of the digestion of bread.

**Secretogogues**—Any substance which is capable of stimulating the gastric glands is termed a SECRETOGOGUE, and it is found that all foods may be divided into **two classes** in this connection; 1, those that contain **ready made sceretogogues** when they enter the stomach, and 2, those that do **not contain secretogogues ready made but which produce them in the early stages of digestion.** To the first group belong all meats, meat extracts and soups; to the second, bread, starchy foods, white of egg, etc.

**Gastrin**—These secretogogues do not act directly on the fundic and prepyloric glands; they stimulate the glands at the pyloric end to produce a hormone termed GASTRIN or GASTRIC SECRETIN. This substance does not escape into the stomach but is absorbed into the bloodvessels and carried in the blood stream to the glands of the fundus and prepylorus which it excites and which then pour out the gastric juice.

THE HORMONES to which this gastrin belongs form a very important group of substances which will be considered later, in connection with intestinal digestion.

**The normal mechanism of gastric secretion then seems to be somewhat as follows:** The secretion of gastric juice is first started by the presence of food in the mouth, and by the pleasant senations and feelings associated with the act of eating (Psychic secretion), the gastric secreting center being acted on by the higher cerebral centers and reflexly from the mouth. This ensures, at least, the BEGINNING OF GASTRIC DIGESTION. Then the secretion is further carried on by the SECRETOGOGUES OF THE FOOD in the stomach; meats and soups contain these ready made, as we have seen, and in the case of other foods they are produced in the early stages of digestion. These act indirectly through the hormone gastrin. Once started the chemical secretion is continued as long as the stomach contents require it.

Although meat (proteins) and starchy foods (carbohydrates), partially digested, stimulate the secretion of gastric juice, fat appears to have a tendency to inhibit it.

According to the researches of Pawlow it would appear that the character of the food determines both the quantity and the quality or strength (percentage of HCl and pepsin present) of the juice, although the quantity is also related to the amount of food to be digested. The secretion produced by bread, although smaller in quantity than that caused by meat, has a stronger digestive power. In fact, the juice secreted is that best adapted to digest the particular kind of food substance which produced its secretion.

The gastric juice has ANTISEPTIC PROPERTIES because of the hydrochloric acid present, so that putrefactive changes do not take place in the normal stomach. Also, pathogenic micro-organisms, swallowed in the food, may be destroyed in the stomach on this account.

### Movements of the Stomach

In seed-eating birds, which are not provided with teeth, the contractions of the muscular walls of the stomach or gizzard are very powerful and serve to grind the food; this takes the place of mastication in the mouth. In man the muscular contractions are too feeble to produce any effect of this kind, and it is not required, if the food has been properly chewed; what these contractions do accomplish is to move the food towards the pyloric end.

The movements of the stomach are best studied with the aid of the X rays after a meal containing some salt of BISMUTH has been taken.

After the food enters the stomach the fundic end becomes TONICALLY CONTRACTED and presses the contents towards the pylorus. When the digestion of part of the food has reached the secondary proteose stage, i. e. about twenty minutes after the food has entered the stomach, a local constriction of the wall appears in the prepyloric region, and a PERISTALTIC WAVE moves toward the pylorus sweeping this portion of the partially digested food or chyme in front of it. [CHYME is the term applied to the partially digested contents of the stomach which pass into the duodenum.] When it reaches the pylorus the SPHINCTER OPENS and lets it through into the duodenum, after which the SPHINCTER CLOSES again. As digestion proceeds this is repeated every few minutes until the stomach is empty.

The opening and closing of the pyloric sphincter muscle is REFLEX; acid on the stomach side opens it and acid on the duodenal side closes it.

The time taken to empty the stomach varies according to the size and digestibility of the meal, the activity of the juice, and the state of the mind and body of the individual. Under normal conditions it varies from three to five hours.

Water, which does not require to be digested, is sent into the duodenum in jets by the same mechanism very shortly after it enters the stomach.

**Nervous Control of Movements**—While the movements of the stomach are automatic they are controlled from two centers in the nervous system, the **excitatory fibers** being contained in the **vagus** and the **inhibitory fibers** in the **splanchnic nerves.** Cannon found that in cats the emotions of rage and fear put an end to all stomach movements and the same probably occurs in man.

It is found from experience that digestion proceeds best in the absence of severe mental and muscular exercise, the reason being that when actively secreting the stomach needs much blood, and under the conditions above mentioned, this is taken by the brain and the muscles.

Very little absorption (passage of material into the blood or lymph) takes place in the stomach; the intestine is the great organ of absorption.

**Hunger Contractions**—After the stomach has been empty for some time "hunger pains" are felt. These are believed to be caused by more powerful contractions of the stomach wall than those already described, since they appear simultaneously with the hunger sensations. Studying these hunger contractions on a man with a permanent gastric fistula, Carlson finds that they are arrested by mechanical stimulation of the gastric mucous membrane, or by the chewing or tasting of palatable food.

**Vomiting**—In vomiting the contents of the stomach are forcibly expelled through the cardiac orifice into the œsophagus and mouth. This is brought about mainly by the action of the DIAPHRAGM AND ABDOMINAL MUSCLES but the stomach itself is not passive; an antiperistaltic wave appears and sweeps the contents towards the cardiac sphincter, which opens reflexly and allows them to escape, the pylorus at the same time being tightly closed.

THE RETCHING MOVEMENTS associated with the act of vomiting are produced as follows: A deep inspiration is taken and the glottis closed to keep the diaphragm depressed; then the abdominal muscles are powerfully contracted, to compress the stomach against the diaphragm, and so squeeze out its contents.

**Vomiting Center**—Vomiting is INVOLUNTARY and REFLEX. The nerve center controlling it is situated in the medulla oblongata, and afferent nerve fibers, from various sources, convey impulses to this center which excite it. Efferent impulses are then discharged from the center to the diaphragm, muscles of the abdominal wall and of the stomach wall, and the act is brought about.

**Causes of Vomiting**—Irritation of the mucous membrane of the stomach is the most common cause; the afferent or sensory nerve fibers, which run in the vagus, are excited and reflexly stimulate the vomiting center. Stimulation of other sensory surfaces, however, will bring it about, e. g. tickling the mucous membrane at the back of the throat.

DISTURBANCES IN THE SENSE OF EQUILIBRIUM by impressions coming in from the semicircular canals frequently result in vomiting, e. g. in sea-sickness and in air-sickness. The vomiting center is also acted on from the CEREBRUM since the mere recollection of

a disagreeable sensation, such as a disgusting odor, will induce the act.

Vomiting is usually, but not always, preceded by a feeling of nausea and accompanied by a flow of saliva into the mouth. During the retching movements which follow, the openings into the trachea and nasal cavities are closed reflexly, as in the case of swallowing.

**Emetics** are substances which induce vomiting. Some act by irritating the gastric mucous membrane, e g. mustard; others, such as tartar emetic and apomorphine by exciting the vomiting center in the medulla oblongata to which they are carried by the blood stream. The latter are more effective when injected hypodermically than when taken by the mouth.

## DIGESTION IN THE INTESTINE

The intestinal tube, in the human subject, is about 30 feet in length—small intestine about 23 feet and large intestine from 5 to 6 feet. The ileo-colic valve, which is a fold of the mucous membrane that plays the part of a valve, and allows the intestinal contents to pass in only one direction, separates the small from the large gut, and the sphincter ani closes the external opening of the latter.

### Small Intestine

**The Small Intestine** is divided, more or less artificially, into THREE parts. The first 10 or 12 inches next to the stomach is termed the **duodenum,** the first two-fifths of the remainder the **jejunum** and the last three-fifths the **ileum.**

**Structure**—In general it resembles the structure of the stomach. It consists of four coats. Externally is the **peritoneum,** and next to this the **muscular coat** consisting of an OUTER LONGITUDINAL and an INNER CIRCULAR LAYER, both composed of plain muscle fibers. Then comes the **submucous coat** made up of connective tissue which carries the larger blood-vessels, nerves and lymphatics. The innermost coat is the **mucous membrane** which contains the secreting glands; between it and the submucous coat is a layer of non-striped muscle termed the MUSCULARIS MUCOSÆ which sends some strands into the villi and between the glands of the mucosa. Between the two layers of the muscular coat is found a network of nerve fibers and cells termed AUERBACH'S PLEXUS, and a similar network—MEISSNER'S PLEXUS—lies in the submucous coat.

**Valvulæ Conniventes**—When the two are separated, the tube of mucous membrane is longer than the muscular tube in which it is placed, and so the former is thrown into a series of transverse folds termed VALVULÆ CONNIVENTES. They serve to increase the

surface of the mucous membrane. They begin about two inches beyond the pylorus and disapppear about the middle of the ileum so that the lower part of the small intestine is free from them.

**Villi**—Examined under the microscope a section of the small intestine shows long slender processes projecting from the free surface of the mucous membrane into the lumen of the gut. These are termed villi and also serve to increase the surface. Each **villus** is lined on the outside by a single layer of COLUMNAR EPITHELIAL CELLS with a striated hem at the free border; here and there clear mucin secreting cells, sometimes termed goblet or CHALICE CELLS, are scattered amongst the others. In the center of the villus is a lymphatic vessel with a blind end termed a LACTEAL and in close relation to it is a network of SMALL BLOOD-VESSELS. Strands of PLAIN MUSCLE FIBERS pass up into the villus from the muscularis mucosæ and there is a loose CONNECTIVE TISSUE frame work with many LEUCOCYTES scattered throughout.

**Glands of Small Intestine**—The mucous membrane contains a large number of simple test-tube like glands lying closely packed, side by side, in the spaces between the villi and lined by a single layer of cubical or low columnar epithelium, along with some chalice cells, continuous with that covering the villi; these are termed the **glands** or **follicles of Lieberkuhn,** and they are found throughout the whole extent of the small and large intestine until the rectum is reached. In the duodenum in addition to the glands of Lieberkuhn there is a number of small compound tubulo-saccular glands situated in the submucous coat; their ducts pierce the muscularis mucosæ and open on the surface of the mucous membrane; these are termed **Brunner's glands.**

**Solitary Glands and Peyer's Patches**—Throughout the mucous membrane there are scattered, at irregular intervals, collections of lymph follicular tissue similar in structure to the tonsil; they are termed SOLITARY GLANDS. In certain regions, particularly the lower part of the ileum, the follicles are aggregated together to form larger masses which are known as AGMINATED GLANDS OR PEYER'S PATCHES. They measure half an inch or more in width and from one to four inches in length, and number in all about thirty. They are very prominent in young people and may be absent altogether in the aged. They do not occur in the large intestine.

## Large Intestine

**The Large Intestine** begins at the ileo-colic (or ileo-cœcal) valve where the small intestine opens into it, which it does from the side, at some distance from its blind end. This blind end is termed the cœcum and from it there projects a tube-like process, about

4 inches in length, and about the thickness of a pencil, the vermiform appendix.

The large intestine is divided into the **cœcum** with **vermiform appendix,** the **colon** and the **rectum.** The colon begins at the right side of the abdomen, a little above the inguinal or groin region, and is subdivided into the ascending, transverse and descending colon with the heptic, splenic and sigmoid flexures. The **ascending colon** runs upwards until it meets the lower surface of the liver; here it bends to the left forming the **hepatic flexure** and crosses the abdominal cavity at a slightly lower level than the stomach; this division is called the **transverse colon.** When it reaches the spleen, to the left of the stomach, it turns downwards at the **splenic flexure** and is now known as the **descending colon;** it terminates in the left groin, in the **sigmoid flexure,** which is continued into the **rectum.**

**Structure of Large Intestine**—In structure the large intestine resembles the small in most respects. It has the same number of coats—peritoneal, muscular, submucous and mucous—but the lumen is much larger. The outer or longitudinal layer of the muscular coat is not continuous all the way around, but is gathered into THREE BANDS, which are shorter than the walls of the tube itself, and this leads to a characteristic puckering of the large intestine. These longitudinal muscular bands are not present in the rectum, where the outer layer is continuous. At the external opening of the rectum (the anus) the muscular coat is increased in thickness so as to form a sphincter similar to that at the pylorus. This is termed the SPHINCTER ANI; it is normally in a state of tonic activity and keeps the orifice firmly closed, unless when it is voluntarily relaxed, in the act of defecation.

In the large intestine there are no valvulæ conniventes and no villi. The mucous membrane is studded with Lieberkuhn's follicles similar to those of the small intestine except that they contain a greater number of mucin secreting or goblet cells.

There are two large and important glands connected with the intestine, viz.: the pancreas and the liver.

## Structure of Pancreas

The pancreas or sweetbread is an elongated, soft organ, of a pinkish color, lying along the lower border of the stomach, and extending from the spleen to the duodenum. It is a COMPOUND TUBULAR GLAND, very similar in structure to the parotid (one of the salivary glands). It is surrounded by a connective tissue CAPSULE which sends in SEPTA subdividing the gland into LOBES and LOBULES. The SECRETORY ALVEOLI open into the lobular ducts, these into the lobar ducts and these again into the main duct which enters the duodenum from three to four inches below

the pylorus, along with the common bile duct from the liver. In some animals, e. g. the dog, there are two pancreatic ducts.

**Islets of Langerhans**—In addition to those lining the secreting tubules, other groups of epithelial cells are found, scattered throughout the gland, which are known as the ISLETS OF LANGERHANS. They are believed to produce an **internal secretion** which is passed directly into the blood or lymphatic vessels and has no relation at all to the process of digestion. They are believed to produce the substance insulin which is essential for the proper metabolism of sugar and the want of which leads to diabetes mellitus. This function of the pancreas will be taken up later. The whole organ has a rich blood supply, particularly the islets of Langerhans.

## Structure of Liver

The liver is the largest gland in the body and weighs from 50 to 60 ounces in the adult. It is of a darkish red color and lies immediately under the diaphragm, the greatest mass of it being to the right side of the middle line. It is surrounded by a delicate connective tissue CAPSULE from which SEPTA pass inwards dividing the organ into a large number of **minute polyhedral lobules.** Each lobule, which is a miniature liver in itself, has a VEIN in its center and is made up of a great number of **hepatic cells** arranged in rows radiating from the central vein, the adjacent rows being separated by **blood capillaries.** In these cells the **bile capillaries** take origin.

**Blood Supply of Liver**—As we have already seen when dealing with the circulation, the blood from the stomach, upper part of intestine, pancreas and spleen enters the liver by the portal vein. This branches like an artery and ultimately breaks up into the intralobular capillaries just mentioned. From these the blood passes into the central or intralobular vein, then into the hepatic veins which open into the inferior vena cava. Many important changes are effected in the portal blood in its passage through the liver.

**The hepatic artery** is a small vessel, a branch of the aorta, which carries blood to the liver to nourish its connective tissue frame work. It corresponds in function to the coronary arteries of the heart, and the bronchial arteries in the lungs.

**The bile capillaries** take origin in the hepatic cells, and in each lobule they form a network of very fine vessels. Through these capillaries the bile, which is the secretion of the liver, formed by the hepatic cells, finds its way into the smaller bile ducts at the periphery of the lobules, and from these into larger and larger ducts until at last it escapes from the liver, through the **hepatic duct,** and passes either into the gall bladder through the **cystic duct,** or into the duodenum through the **common bile duct,** the last being formed by the union of the hepatic and cystic ducts.

## Digestive Secretions that Enter the Small Intestine

The secretions poured into the small intestine are three in number: 1, the **pancreatic juice** from the pancreas; 2, the **intestinal juice** (succus entericus) from the glands of the small intestine; 3, **bile from the liver.**

### Pancreatic Secretion

This may be obtained pure by making a **pancreatic fistula,** i. e. tying a glass tube into the duct, in an anæsthetized animal such as a dog, and collecting the juice in a beaker as it flows (temporary fistula); or by stitching the orifice of the DUCT to an opening in the abdominal wall and allowing the wound to heal (permanent fistula). In the latter case the secretion will be poured out on the exterior and may be caught by attaching a clean sponge, or a vessel of some kind, to the abdomen.

It has also been collected in the human subject in cases of tumour, involving the duodenum, where it was necessary to drain off the secretion to the exterior.

**Characters of Pancreatic Juice**—It is a clear, colorless, slightly viscous fluid, somewhat resembling saliva, with a strongly alkaline reaction due to the presence of sodium carbonate. Its important constituents are three ENZYMES OR FERMENTS: 1, **steapsin,** (pancreatic lipase) or fat-splitting ferment; 2, **amylopsin,** (pancreatic amylase) or starch-splitting ferment; 3, **trypsin,** (pancreatic protease) or protein-splitting ferment. The pancreatic juice therefore has an ACTION ON ALL THREE CLASSES OF FOOD STUFFS. There is also present pancreatic rennin, lactase and maltase.

**Action on Fats**—The neutral fats (stearin, palmitin and olein) are compounds (esters) of glycerin in which the three hydroxyl groups are replaced by fatty acid radicles (For formulæ see board). Under the influence of the ferment **lipase** the fats are hydrolyzed, that is, water is added and the molecule then splits up into GLYCERIN and the corresponding FREE FATTY ACID.

A portion of the fatty acid produced in this way combines with the alkali sodium carbonate to form **soaps** which, acting along with the bile, helps to **emulsify the fat** still undecomposed, that is, to break it up into fine globules so that it is more easily reached by the ferment. At one time it was believed that this emulsification was all that was necessary and that the fine fatty globules were absorbed as such by the intestinal epithelium, but now it is held that all the fat is decomposed into glycerine and free fatty acid which are absorbed, and in the process of absorption, while still within the epithelial cells, are recombined to form again the neutral fats characteristic of the animal.

**Action on Carbohydrates**—The action of the ferment **amylopsin** is believed to be identical with that of the ptyalin of saliva; it

CONVERTS STARCH INTO MALTOSE with dextrin as an intermediate product. Starchy foods, therefore, which have escaped digestion in the mouth and stomach, are completely transformed into the reducing sugar maltose in the intestine. The maltose is then acted on by the ferment maltase, of the succus entericus, and changed to glucose, the form in which all carbohydrates are absorbed into the blood.

**Action on Proteins**—The ferment **trypsin,** acting in an ALKALINE MEDIUM, transforms coagulable proteins, such as egg albumin, into proteoses and peptones like the pepsin of the gastric juice, but here the action goes farther than the peptone stage. By a process of hydrolysis the proteins are split up into a number of substances of low molecular weight belonging to the group of **amino-acids,** examples of which are LEUCIN, TYROSIN, ASPARATIC ACID, and many others. These comparatively simple substances (see formulæ on board) are absorbed by the epithelium lining the intestine, pass into the blood stream directly or through the lacteals, and are again built up into the protein molecules of the animal which digests them. Where this reconstruction takes place is not certain; it may be in the blood or in the tissues themselves, probably the latter.

The action of trypsin is more rapid and more complete following peptic digestion.

**Activation of Trypsin**—Pure pancreatic juice, as it is obtained from a pancreatic fistula, has no digestive action on proteins, but when a fragment of mucous membrane from the small intestine is added to it, it becomes active. The reason for this is as follows: Pancreatic juice when it escapes from the duct contains no trypsin, only the zymogen or pro-substance **trypsinogen** is present which has no power to hydrolyze protein. In the small intestine the trypsinogen meets with a ferment **enterokinase,** contained in the intestinal secretion, and this converts the inactive trypsinogen into active trypsin which then attacks the protein molecule.

**Changes in Secreting Cells of Pancreas**—In the inactive or resting stage granules accumulate in the cells lining the tubules; these are discharged during secretory activity, just as we have seen in the case of the salivary glands. It is probable that these granules represent the zymogens or pro-substances which are the precursors of the active ferments found in the juice.

## Mechanism of Pancreatic Secretion

The pancreatic juice does not flow continuously into the small intestine. The secretion begins about half an hour after food enters the stomach and attains its maximum rate in from two to four hours. It flows intermittently until pancreatic digestion is

complete, and then it almost ceases. There is little or no flow while fasting.

The stimulus that excites the pancreas to pour out its secretion is known to be the PRESENCE OF ACID CHYME IN THE DUODENUM. Dilute acid such as HCl, injected into the duodenum, will produce a flow at any time. Until recently this was believed to be simply a nervous reflex, through a supposed pancreatic secretory center in the medulla oblongata; such, however, is not the case, since pancreatic secretion can take place after all the nerves to the intestine have been divided, that is, the reflex arc interrupted. THE STIMULATION IS ENTIRELY CHEMICAL. What happens is that the acid acts on a substance, contained in the mucous membrane of the small intestine, termed **pro-secretin** and converts it into **secretin** which is absorbed into the blood vessels and carried in the blood stream to the pancreas, where it excites the cells lining the tubules to pour out their secretion.

This substance secretin can be prepared artificially as follows: Scrape the mucous membrane from the duodenum and upper half of the jejunum of a recently killed dog and mix it with 100 c.c. or 200 c.c. of 0.4% HCl. Allow this to stand for a few hours; neutralize, boil and filter; the filtrate will contain secretin. A small quantity of this filtrate, injected into a vein, will cause a flow of pancreatic juice in about 20 seconds, that is, as soon as it reaches the pancreas in the blood stream.

## Hormones

Secretin, and its action on the pancreas, was discovered by Bayliss and Starling and it belongs to the same group as gastrin, which we have seen is produced in the pyloric end of the stomach. To substances of this class Starling has given the general name of HORMONES or exciters. Many others are now known to exist. A hormone may be defined as a CHEMICAL SUBSTANCE PRODUCED IN ONE PART OF THE BODY AND CARRIED IN THE BLOOD STREAM TO SOME OTHER PART WHICH IT EXCITES TO ACTION; for example, secretin, produced in the mucous membrane of the small intestine, and carried in the blood stream to the pancreas, which it excites to action.

Chemically the hormones are comparatively SIMPLE SUBSTANCES of low molecular weight and HEAT STABLE since they are not decomposed by boiling as all ferments are. They are rapidly oxidized in the tissues, however, and rendered inert after they have accomplished their purpose. They play a very important rôle in the body, taking the place of the nervous system in correlating the activity of associated tissues and organs, where there is no great necessity for speed.

It is interesting to observe that in the salivary glands the excit-

ing stimulus is entirely nervous, in the stomach partly nervous and partly chemical, and in the pancreas almost entirely chemical but the possiblity of some nervous influence cannot be completely excluded.

### Intestinal Secretion

This is produced by the intestinal glands. To obtain it free from the products of digestion a fistula must be made in the intestine by one of two methods. By **Thiry's method** a piece of intestine about six inches long is cut out, without damaging its blood or nerve supply; one end is sewed up and the other stitched to the abdominal wall. This blind piece of gut is then washed out and the secretion collected when it accumulates. In **Vella's** modification of Thiry's method, both ends of the loop are stitched to the abdominal wall.

Pure intestinal juice (Succus entericus), when thus procured, is a turbid fluid, alkaline in reaction, the turbidity being due to leucocytes and disintegrated epithelium. It contains the following important enzymes: 1, **Enterokinase** which activates trypsinogen; 2, **Erepsin** which assists the trypsin of the pancreatic juice in splitting up peptones into amino acids; 3, **Enzymes,** three in number, which convert **carbohydrates of all varieties into glucose,** the form in which they are finally absorbed.

### Liver Secretion

The third secretion which acts on the chyme in the small intestine is bile from the liver. The common bile duct, formed as we have seen by the union of the hepatic and cystic ducts, opens into the duodenum very obliquely, and this serves as a VALVE to prevent the entrance into the duct of matter from the intestine.

Unlike the pancreatic juice the BILE IS BEING CONTINUOUSLY SECRETED by the liver cells, but it does not flow directly into the duodenum; it is stored up, during fasting, in the gall bladder, and is only discharged when acid chyme comes into the duodenum from the stomach; it is not all expelled at once. The cause of this expulsion is the reflex stimulation of the muscular walls of the gall bladder by the contact of acid with the duodenal mucous membrane. Some animals, such as the horse and deer, have no gall bladder and in these the flow into the intestine is continuous. Secretin excites the liver as well as the pancreas. The bile and pancreatic juice coöperate in their action on the chyme and they are discharged into the duodenum together.

**Bile** may be obtained in the usual way by establishing a **biliary fistula,** that is, by stitching the bile duct or the gall bladder to the abdominal wall and collecting the secretion as it escapes. It may also be secured by emptying the gall bladder of a recently killed

animal. In the human subject it is sometimes necessary, in cases of obstruction of the common bile duct, to establish a biliary fistula through the gall bladder. In such cases the amount collected varies from 500 c.c. to 800 c.c. in the 24 hours.

**Physical Characters of Bile**—It is a viscid, yellowish, reddish-brown or green fluid, according to the preponderating pigment present. It has a peculiar characteristic odor, a bitter taste ("bitter as gall"), and is alkaline in reaction. The viscidity is due to the presence of MUCIN and this is added to the bile in the gall bladder; bile collected from the hepatic duct contains little or no mucin.

**Composition of Bile** (see board)—The solids total from 2 to 3 per cent., 97 to 98 percent. being water. The chief constituents are the salts of the bile acids (glycocholic and taurocholic acids), cholesteroe, bile pigments, lecithin, mucin and mineral salts. The composition varies considerably in different samples. The BILE PIGMENTS ARE DERIVED FROM THE HÆMOGLOBIN of broken down red blood corpuscles. The usual golden red of human bile is due to the preponderance of the red bile pigment or **bilirubin,** while the green color of herbivorous bile is caused by the pigment **biliverdin** which is an oxidation product of bilirubin. Another oxidation product is the yellow pigment **choletelin.** One of the chemical tests for bile consists in the production of this play of colors by the action of strong oxidizing agents such as fuming nitric acid.

**Functions of Bile**—1. It is alkaline and helps to NEUTRALIZE THE ACID CHYME and so prepare the way for pancreatic digestion, which takes place best in an alkaline medium. 2. Another important property is its power to EMULSIFY FATS, that is, to split them up into fine globules so that the ferment steapsin may act more readily and effectively on them. If the common bile duct is obstructed, preventing the entrance of bile into the intestine, a large amount of fat is found free in the excreta because it has not been emulsified. The presence of bile in the intestine favors the action of all the pancreatic enzymes but more especially that of lipase which is due to the emulsifying power of bile salts. The fine subdivision of the fat globules enables the lipase to act more effectively. 3. It is said to STIMULATE THE PERISTALTIC MOVEMENTS OF THE LARGE INTESTINE.

**Jaundice**—This is most commonly caused by some obstruction in the bile duct with the result that the bile, which is normally secreted at a low pressure, is dammed back in the liver and absorbed by the lymphatics and blood-vessels into the general circulation. It is the presence of bile in the blood that gives the greenish yellow tinge to the skin and mucous membrane characteristic of jaundice.

## Movements of the Intestines

These are of two kinds, peristaltic and segmental. By the former the intestinal contents are slowly driven down the gut, from the small to the large intestine. The **peristaltic movements** are produced as follows: On the stomach side of a mass of food the intestine becomes constricted, by the contraction of its inner muscular coat, and on the rectal side of the mass it dilates, an example of the "law of the intestine" as shown by Bayliss and Starling. In this way the food is moved downwards by these waves preceding and following it. The other kind of movement (**segmental**) is due to ring like constriction that take place rhythmically at regular distances apart. They do not propel the contents downwards, but break them up into segments, so that the digestive juices may have more ready access to them.

It is estimated, from observations made on the human subject by the X-rays, that the time required for the passage of the food through the small intestine is about 4½ hours. This is about the time it takes to digest an ordinary meal, so that when the last of it is being expelled from the stomach, into the duodenum, the first of it has reached the ileo-colic valve. All the food, completely digested and partially digested, which has not been absorbed, will be found in the small intestine at one time, viz.: about 4½ hours after a meal.

The contents of the small intestine, after being acted on by the succus entericus, pancreatic juice, and bile are passed on into the large intestine. Here the downward movement is much slower. It takes the contents 6½ hours to reach the hepatic flexure of the colon, 9 hours to reach the splenic flexure, 12 hours to arrive at the upper end of the sigmoid flexure, and 18 hours to reach the rectum.

The products of digestion are absorbed, for the most part, in the small intestine, mainly in the lower part of the ileum. The contents are liquid when passed into the large intestine but there much of the water is absorbed, particularly in the cœcum, and they soon become semi-solid.

In the large intestine **putrefactive changes** take place, due to the presence of BACTERIA, and many substances are formed as END-PRODUCTS which are discharged in the excreta. Important amongst these are **indol** and **skatol** which give the characteristic offensive odor to the fæces.

If the contents remain in the large intestine for any length of time, these substances are ABSORBED INTO THE BLOOD and act in a DELETERIOUS MANNER ON THE WHOLE SYSTEM, giving rise to general malaise, headache, etc.; hence the necessity of preventing constipation.

In habitual constipation the whole body is being systematically poisoned from the large intestine.

### Mechanism of Absorption from Small Intestine

The digested materials—glucose, glycerine and fatty acids, and the end products of protein digestion, mainly amino acids—pass through the columnar epithelium lining the villi, into TWO SETS OF VESSELS,—**lacteals** (lymphatic vessels) and **blood capillaries.** Even if the proteoses and peptone are to a slight extent absorbed they are so changed by erepsin in the mucous membrane of the intestinal wall that the only substances resulting from the digestion of proteins which reach the blood are the amino-acids.

THE GLYCERINE AND FATTY ACIDS ARE PROBABLY RECONSTRUCTED INTO NEUTRAL FATS IN THEIR PASSAGE THROUGH THE EPITHELIUM, and these are carried into the LACTEALS. It would appear that the intestinal mucous membrane has the power of modifying the composition of fat during its absorption. The fat globules are seized by **leucocytes** and conveyed by these into the lacteals, the contents of which are ultimately discharged, by the THORACIC DUCT, into the great veins at the root of the neck. When chyle is collected from a fistula in the thoracic duct only about 60% of the fat known to be ingested with the food is recovered. Over 90% of the food fat is normally taken up from the intestine. The question as to what becomes of the 30% unrecovered has not been adequately answered.

The sugar (glucose) and protein products (mainly amino-acids) pass, for the most part, DIRECTLY INTO THE BLOOD-VESSELS.

All the substances absorbed into the blood vessels of the villi pass through the liver before they reach the general circulation.

If the sugar (glucose) content of the blood rises to about 0.3%, THE EXCESS IS EXCRETED BY THE KIDNEY, AS A FOREIGN SUBSTANCE, and lost to the body. One reason why the liver is placed on the portal circulation is to prevent too much sugar getting into the blood, at one time, so that it may not be thrown away by the kidneys.

Water is absorbed throughout the whole intestine but mainly in the large. The amount which disappears in the small intestine is not sufficient to affect greatly the fluidity of its contents because the secretions being poured into the gut just about make up for the water absorbed. Absorption of water from the large intestine is much more noticeable since the contents here are semi-solid or even hard feces whereas in the small intestine they are always fluid.

### Glycogenic Function of the Liver

The LIVER CELLS DEHYDRATE THE GLUCOSE brought to them in the blood of the portal vein and convert it into GLYCOGEN or animal starch. This process is the reverse of what takes place in the mouth, stomach and intestine.

This glycogen is stored up in the liver cells, then gradually reconverted into glucose, and given out in small quantities to the blood, as it is required.

These facts were discovered by Claude Bernard.

**The liver is the regulator of the supply of sugar to the blood** and it strives to keep it constant, and below the point where it will be thrown off by the kidneys. Usually it does not rise above 0.1 per cent. Glycogen is also formed in other situations, chiefly in muscle particularly of cold blooded animals. It occurs in traces in most animal tissues.

There is a relationship between the internal secretion of the pancreas and the carbohydrate changes in the liver.

### Formation of Urea by the Liver

IN THE METABOLISM OF THE AMINO-ACIDS SOME AMMONIA COMPOUNDS ARE FORMED, and these, if allowed to accumulate in the circulation (where they probably exist as ammonium carbonate or carbamate), WILL ACT AS POISONS. They must therefore be removed, and their removal is believed to be effected by the liver, which converts them into the comparatively harmless substance **urea.** This is then excreted by the kidneys.

The transformation is brought about by a process of dehydration, thus:

$$\begin{array}{lll} \text{Ammon. Carbamate} & & \text{Urea} \\ \text{CO}\left\langle\begin{array}{l}\text{ONH}_4\\ \text{NH}_2\end{array}\right. & -\text{H}_2\text{O} = & \text{CO}\left\langle\begin{array}{l}\text{NH}_2\\ \text{NH}_2\end{array}\right. \end{array}$$

or

$$\begin{array}{lll} \text{Ammon. Carbonate} & & \\ \text{CO}\left\langle\begin{array}{l}\text{ONH}_4\\ \text{ONH}_4\end{array}\right. & -2\text{H}_2\text{O} = & \text{CO}\left\langle\begin{array}{l}\text{NH}_2\\ \text{NH}_2\end{array}\right. \end{array}$$

**Proofs that Urea is Formed in the Liver** and not in the kidney. Urea is the chief end-product in the metabolism of proteins, and is excreted in large quantity in the urine, being its principal organic constituent. At one time it was supposed that the urea was produced in the kidney, but that is no longer believed.

That urea is formed in the liver has been proved in several ways.

1. The total extirpation of the liver is such a severe operation, in mammals, that they do not usually survive it, but in the frog it is otherwise. In a frog, from which the liver has been removed, urea disappears from the urine and ammonium compounds take its place.

2. It is possible in mammals to cut the liver out of the circulaton by uniting the portal vein to the inferior vena cava, so

that the blood from the stomach, intestine, etc., does not pass through the liver at all, but flows directly into the vena cava. This is known as an **Eck fistula.** Here again, urea is to a large extent absent from the urine, and ammonium salts are greatly increased.

3. In extensive disease of the liver, in the human subject, urea is diminished in the urine and ammonium salts correspondingly increased.

4. If the liver be removed from a freshly killed animal, and perfused through the portal vein with defibrinated blood to which ammonium carbonate or carbamate has been added, the blood, as it escapes from the hepatic veins, will contain urea, and some of the ammonium salts will have disappeared. If the kidney be perfused in the same way with normal blood, to which the salts of ammonium have been added, no urea will be present in the blood as it escapes from the organ and there will be no loss of ammonium salts.

Some urea is formed in the muscles and other tissues, but it appears to be the special function of the liver to transform the poisonous ammonium compounds produced in the intestines into the harmless substance urea.

## BODY METABOLISM

All the chemical transformations which the food substances undergo, from the time they are absorbed from the alimentary canal until thrown off in the excretions, are included under the term **body metabolism.** The oxygen taken in from the lungs must also be considered as a food substance, in this relation. In these metabolic processes the chemical changes are of two kinds—**katabolic** and **anabolic;** the tissues are constantly being broken down into simpler compounds (katabolism) and at the same time the loss is being made good by the building up of new tissue material from the nutrient substances brought in the bloodstream (anabolism).

It must be remembered that only from 90 to 95 per cent. of the food taken into the stomach is digested and absorbed into the blood; the remainder is thrown off in the fæces and simply passes through the body taking no part in tissue metabolism.

**Food Substances the Source of Body Heat**—The heat of the body is produced by the oxidation of the food substances after they have been digested and have entered the tissues. The heat produced by the complete oxidation of a food-stuff may be determined by burning a known quantity of it in a **bomb calorimeter.** For a description of this instrument, see p. 136.

The amount of heat produced by the complete oxidation of one gram of any food-stuff is known as its **caloric or heat value.** If one gram of fat is burnt in a bomb calorimeter it will yield 9.3 large calories of heat, one gram of carbohydrate, 4.1 calories and one gram of protein 5.6 calories. These figures represent the **physical heat values** of fat, carbohydrate and protein. The **physiological heat value** is the amount of heat given out by the food substance when oxidized in the body. The physical and physiological heat values of fats and carbohydrates are identical, because these are completely oxidized in the body, but the physiological heat value of protein is less than its physical heat value, since it is not completely oxidized in the body. One of the end-products of the protein molecule is urea which is incompletely oxidized and still capable of yielding a considerable amount of heat, so that one gram of protein oxidized in the body yields only 4.1 calories.

The physiological heat values of the food substances are as follows:

| | |
|---|---|
| Fat | 9.3 calories |
| Carbohydrate | 4.1 calories. |
| Protein | 4.1 calories |

The energy liberated in the body by the oxidation of the food takes the form partly of heat and partly of muscular work. Enough food is required to produce daily about 3000 calories of heat.

In attempting to trace the successive changes through which the food substances pass from their entrance into the body to their elimination from it, great difficulties are met with, since, although we can determine by analysis their chemical composition when ingested and that of their end-products when thrown off, we have little means of knowing the intermediate stages in the transformations.

## Metabolism of Fat

The fats, after being digested in the alimentary canal, that is, split up into glycerine and free fatty acid, are rebuilt up in the process of absorption by the epithelium lining the small intestine, and enter the blood stream through the **thoracic duct.** From the blood the fat is stored up, for the most part, in the subcutaneous tissue, omentum and other situations, where it serves as a reserve stock of fuel, the small proportion needed for immediate use passing directly to the tissues.

When required the stored fat is drawn upon, but it cannot be used directly by the muscles and other tissues; it must first undergo certain changes in the liver, to which it is carried by the blood of the portal vein. These changes consist in desaturating the higher neutral fats so that they may be broken up into the lower fatty acids (e. g. caproic and butyric) and finally oxidized into carbon dioxide and water.

When an individual neither gains nor loses in weight the fat stored, after a meal, is all used up before the next meal; if weight is lost the reserve of fat is being depleted and if weight is gained more fat is being stored than is used. In starvation the stored fat is used by the tissues as their chief source of energy, all of it passing first through the liver before it can be utilized by them, however. So far as the space which it occupies is concerned fat is a very economical form of energy storage; 12 c.c. of adipose tissue, weighing about 11 grams, will yield about 100 large calories of heat, whereas if this amount of heat were stored in carbohydrate (glycogen) in liver tissue it would require more than ten times as much or 130 grams at least.

**Formation of Fat from Carbohydrate**—In man the fat taken as food is the usual source of the fat of the body, but it can be formed from the carbohydrates of the food, and in the herbivora most of it is so formed. This was proved by the **experiment of Lawes and Gilbert** on the fattening of cattle, sheep and pigs. The food of these animals was analyzed and the amount of fat, carbohydrate and protein determined. On killing them far more fat was found

in their bodies than could be accounted for by the fat of the food; the body fat, therefore, must have been formed from either protein or carbohydrate, but it could not be formed from protein since the quantity of fat in the body was larger than the amount of protein contained in the food; most of it, therefore, must have come from the carbohydrate.

This transformation of carbohydrate into fat cannot be effected in the laboratory, and the process by which the change is brought about in the living body is not understood.

Whether fat can be formed from protein is an open question. The fact that dogs fed on protein diet, free from fat and carbohydrate, do not put on fat would seem to be against this idea.

It is a curious fact that fat cannot be completely oxidized unless carbohydrate is present in the tissue cells. When the tissues are deprived of carbohydrates, as in starvation, or in animals on a carbohydrate-free diet, the final products of the oxidation of fat are not $CO_2$ and water but $\beta$ oxybutyric acid, diacetic acid and acetone which are excreted in the urine as such. This condition is known as **acidosis**; it indicates that the supply of carbohydrates to the tissues is insufficient. Under normal conditions these three substances are believed to be intermediate products in the oxidation of fat, but here the process goes on to the final stage, with $CO_2$ and water as the end-products.

## Metabolism of Carbohydrates

As we have already seen, the carbohydrates of the food are all transformed into glucose before absorption; this enters the blood of the portal circulation and is carried to the liver where most of it is converted into **glycogen** which is stored in the liver cells for future use. While the blood of the portal vein during the digestion of a meal containing carbohydrates may contain a large quantity of sugar, the amount present in the blood of the general circulation normally does not rise above 0.1 to 0.2 percent.; if the sugar in the blood exceeds this it is thrown off by the kidneys and we have the condition known as **glycosuria** (sugar in the urine).

The tissues are always removing sugar from the blood to satisfy their needs, and the blood would soon be depleted of it were it not for the fact that the carbohydrate, stored in the liver as glycogen, is gradually reconverted into sugar which passes from the liver, through the hepatic veins, into the inferior vena cava and keeps the supply up to the normal, viz.: 0.1 to 0.2 percent. These facts were discovered by Claude Bernard.

The transformation of sugar into glycogen in the liver is termed **glycogenesis,** the change in the opposite direction from glycogen into sugar **glycogenolysis,** while the taking up and consumption of sugar by the tissues is known as **glycolysis.** All three changes are

probably due to the action of a ferment or ferments, or, it may be, to hormones. An excessive amount of sugar in the blood (more than 0.2 per cent.) is known as **hyperglycæmia** and this is followed by **glycosuria.**

There exists in the body a mechanism by which these various processes are regulated and adapted to each other, so that the demand by the tissues is always met by the liver and the sugar content of the blood is kept up to the normal, but little is known of its nature. If this regulating mechanism breaks down then, as a rule, hyperglycæmia and glycosuria follow.

**Varieties of Glycosuria**—Sugar in the urine may be due to various causes.

1. **Alimentary Glycosuria** is produced by the consumption of an **excessive amount of sugar** in the food in the form of glucose for it may be present in such quantity in the blood of the portal veins, that the liver is not able to transform the whole of it into glycogen, and much may pass through the liver into the general circulation, producing hyperglycæmia and glycosuria. This may be found in any healthy individual where the liver, pancreas and kidneys are prefectly normal. It is temporary and of no significance. This method of producing glycosuria is sometimes used in malingering.

2. **Adrenalin Glycosuria**—If a small quantity of adrenalin (extract of suprarenal capsule) be injected into the circulation glycosuria will quickly follow. The explanation is that the adrenalin stimulates the liver to transform glycogen into sugar at a greater rate than normal, with the result that an excessive quantity is thrown into the blood. If the liver be examined afterwards it will be found that the glycogen has almost disappeared from it.

3. **Puncture Diabetes of Claude Bernard**—It was discovered by Claude Bernard, long ago, that a slight puncture in the **floor of the fourth ventricle** (medulla oblongata), in the rabbit, is quickly followed by the appearance of sugar in the urine. This was explained by supposing that in this part of the brain a nerve center had been excited, which caused the liver cells to become more active in transforming glycogen into sugar. Now it is held that the effect on the liver is produced **indirectly through the suprarenal capsules;** the nerve stimulation leads to the secretion of **adrenalin** by the capsules, in excessive amount, and this reaching the liver, through the blood, excites the hepatic cells. When the suprarenal capsules have been removed the diabetic puncture fails to produce glycosuria.

4. **Phloridzin Glycosuria**—A small quantity of the drug phloridzin, injected into the blood, leads to glycosuria but this is not preceded by hypergleæmia as is usually the case. The **phloridzin acts on the cells of the kidney** tubules and excites them to secrete sugar when it is present in even less than the normal amount in the blood.

The sugar removed from the blood is replaced by the liver, so that the store of glycogen is rapidly depleted, and after two or three doses, it may disappear altogether.

5. **Pancreatic Glycosuria** or **Experimental Diabetes.** When the **pancreas is completely removed** from animals sugar appears in the urine, within a few hours; they lose weight rapidly and die in a few weeks. They exhibit the same symptoms as are found in the disease known as **diabetes mellitus** in the human subject. The cause of this condition is not the want of pancreatic juice in the small intestine, for when the **pancreatic duct is tied,** or blocked with paraffin, no glycosuria results, nor does it occur if a small piece of pancreas is left behind. The real cause of this condition is the absence of the internal secretion insulin produced by the **islets of Langerhans** which, in the normal animal, enables the tissues, particularly muscle, to utilize the sugar brought to them in the blood. As a result the sugar accumulates in the blood and is thrown off by the kidneys. Certain forms of diabetes mellitus in the human subject are attributed to the same cause, since, in many cases, the islets of Langerhans have been found to be diseased at the post mortem examination.

The carbohydrates of the food are ultimately oxidized to $CO_2$ and water but the intermediate steps in the process have not been followed; it is believed that lactic acid is one of the intermediate products.

**Formation of Carbohydrate from Protein.** We have seen that fat may be formed from carbohydrate in the animal body, but there is no evidence to show that the reverse change takes place, viz., the formation of carbohydrate from fat, unless possibly in hibernating animals. Carbohydrate may be derived from protein, however. In phloridzin glycosuria all the glycogen may disappear from the liver, and when the animal is not receiving any carbodyhrate in its food, sugar is still found in the urine. In this case it is believed to be derived from the tissue proteins; the animal loses weight rapidly.

## Protein Metabolism

The final products of protein digestion are various **animo-acids** and these are absorbed by the intestinal epithelium and pass into the blood as such. Immediately after or during their absorption, part of them are deaminized, that is, lose the animo group $NH_2$, the nitrogen being carried to the liver in the form of ammonium compounds and there transformed into urea.

**The metabolism of proteins** in the body is of two kinds, viz.: exogenous and endogenous. The greater part of the animo-acids, after deaminization, are carried to the tissues and there oxidized into $CO_2$ and water. They never really become a part of the tissue,

but are burnt outside it, thus serving as heat and work producers. This is known as **exogenous protein metabolism.** The end products excreted in the urine are **urea** and the **inorganic sulphates.** A certain proportion of the animo-acids, however, becomes a part of the living tissues, and the changes through which these pass are included in the term **endogenous protein metabolism;** the final products here are **creatinine** and **uric acid.** By estimating the amount of urea and inorganic sulphates in the urine, on the one hand, and the amount of creatinine and uric acid on the other, it is possible to tell approximately, the proportion of food protein to tissue protein.

There are certain animo-acids or combinations of animo-acids that cannot be formed in the body which are essential in the building up of tissue protein, and unless they are present in the food tissue protein cannot be formed. Examples of these are **tryptophane, tyrosine** and **phenylalanine. Gelatine** is a protein, but, as is well known, it will not maintain life and the reason is that it does not contain these groupings. Another protein named **zein,** found in maize, will not maintain life because it contains no tryptophane.

## DIETETICS

The food of man and animals, which consists of **proteins, carbohydrates** and **fats,** together with **salts** and **water,** is required for two purposes, viz.: first, as a **source of energy.** A constant transformation of potential energy, stored up in the food substances, into the kinetic energy of heat and work is taking place in the body and to supply this energy food must be consumed. Second, food is necessary to replace the **tear and wear of the tissues** which are continually breaking down and for this purpose **proteins are essential.**

The energy stored up in all food substances is derived ultimately from the sun. Under the influence of the sun's rays plants possess the power of building up, out of the simple elements carbon, nitrogen, hydrogen and oxygen, etc., complex molecules in which large quantities of potential energy are stored, and these vegetable substances are used either directly or indirectly by animals as food.

**Food as a Source of Energy.** It is found, by actual calorimetric measurement, that a man of average size, doing light work, gives off somewhat less than 3000 large calories of heat in the 24 hours, and if the muscular work, performed in that time, transformed into heat units be added, it will bring the total energy expended up to about this figure, viz.: **3000 kilocalories.** In individuals leading a sedentary life it will be less and in those doing hard muscular work considerably more, over 5000 kilocalories it may be.

If the body weight is to be maintained enough food must be given to supply this energy because it is the oxidation of the food substances within the body which is the source of heat and muscular work. Knowing the **physiological heat values** of the food proximate principles (protein, carbohydrate, fat) we can calculate how many grams is necessary to yield this energy.

**Food to Supply Tissue Waste.** If the body weight is not to fall enough food must be consumed to make good the tissue waste, or, in other words, to replace the **carbon and nitrogen** lost in the excreta (urine, fæces, expired air). The nutritive value of a food depends mainly on the amount of carbon and nitrogen which it contains. A man on ordinary diet and doing a moderate amount of work will eliminate from 250 to 280 grams of carbon in the 24 hours and from 15 to 18 grams of nitrogen. This gives a carbon to nitrogen ratio of about 16.5:1. In muscular exercise the amount of carbon eliminated is greatly increased while the output of nitrogen is scarcely affected, so that in a diet for hard muscular work the carbon to nitrogen ratio should be greater than 16.5:1.

**Protein is essential in all dietaries** since it alone contains nitrogen but a pure protein diet is not suitable because it does not contain enough carbon. The carbon to nitrogen ratio in protein is only 3.5:1, so that when the requisite 15 grams of nitrogen have been taken there will be only 53 grams of carbon instead of the necessary 250 grams. The extra carbon, therefore, must come from fat and carbohydrate.

In arranging a daily diet enough must be given to supply the energy given out by the body in the form of heat and muscular work, to replace the carbon and nitrogen eliminated from the body, and the proportions of the proximate principles must be such that the carbon to nitrogen ratio is not far from 16.5:1. In making up daily diets on this basis enough protein must be allowed first to supply the requisite quantity of nitrogen, and secondly fats and carbohydrates to balance the energy lost. In practice it is found that fats and carbohydrates may be made to replace each other to a considerable extent.

Voit, from a large number of observations on bodies of workmen, body weight 70—75 kilograms, considered the following daily diet adequate.

| | Grams | | Calories |
|---|---|---|---|
| Protein | 118 | yielding | 483 |
| Fat | 56 | " | 520 |
| Carbohydrate | 500 | " | 2050 |
| Total | | | 3053 |

Ranke found that for himself, weighing 74 kilograms and leading a sedentary life, the following diet was sufficient:

| | Grams | | Calories |
|---|---|---|---|
| Protein | 100 | yielding | 410 |
| Fat | 100 | " | 930 |
| Carbohydrate | 240 | " | 984 |
| Total | | | 2324 |

The daily diet allowed by Atwater in America is more generous:

| | Grams | | Calories |
|---|---|---|---|
| Protein | 125 | yielding | 512 |
| Fat | 125 | " | 1172 |
| Carbohydrate | 400 | " | 1640 |
| Total | | | 3324 |

By consulting a table showing the composition of the various food-stuffs a diet may be readily constructed containing the proper proportions of the three proximate principles, in sufficient quantity, but this is not enough. The appetite must be considered, also the digestibility of the various food substances as well as their cost.

For example, vegetable proteins are, as a rule, cheaper than animal proteins but they are less digestible, and fats are dearer than carbohydrates. The tendency is for well-to-do people to use protein in excess while those to whom cost is an important consideration rely most on carbohydrates.

**The Salts and Water.** These in the course of their metabolism give out no energy, yet they are essential articles of diet, since animals fed on an ash-free diet succumb as rapidly as they would have done if deprived of all food, with the exception of water. They enter into the composition of all living protoplasm and are as important, in this relation, as the proteins. The osmotic pressure of the body fluids is due to the presence of salts in solution (mainly sodium chloride) and this plays an important part in the control of the flow of water to and from the tissues. As we have seen, calcium is essential in blood coagulation, and the balanced action of calcium on the one hand and sodium and potassium on the other may be the essential cause of the heart beat. Iron, again, is necessary for the production of hæmoglobin.

The function of water is to act as a solvent.

VITAMINES. These are substances, present in minute quantities in the husks of certain grains, in vegetables, in milk and other foods, which are essential in all diets, if health is to be maintained. Little is known, so far, regarding their chemical nature or composition. Their absence from the diet for a considerable period leads to such diseases as beri-beri, scurry, rickets, and probably pellagra. For example, persons living largely on polished rice, that is rice from which the outer coat or husk has been removed, suffer from a form of neuritis termed beri-beri, and it is now believed that this is due to the **absence of vitamines.** The disease can be cured by using rice from which the outer layers have not been removed, or by adding the polishings, or the alcoholic extracts of them, to the diet of polished rice. In birds a similar condition can be caused by feeding them on polished rice and cured as stated above.

# ANIMAL HEAT

**Historical**—The ancients could give no explanation of the cause of animal heat; it was there in the body and existed per se; it was different, they believed, from the heat given out by inanimate objects and so they called it "animal heat" or "vital heat."

This vital heat was supposed, by Galen, to be produced in the heart and to be distributed through the body by the blood in the veins. It was prevented from accumulating in the heart, to too great an extent, by the cool air taken into the lungs which were placed around the heart for this purpose. The function of respiration, according to him, was concerned with keeping the body cool.

In more modern times, after the discovery of the circulation by Harvey, in the 17th century, when physiologists began, to some extent, to think in terms of physics and chemistry, attempts were made to give a more rational explanation of body heat, and since only two sources of heat were known at that time, viz.: friction and fermentation, they were divided into two schools, the frictionists and the fermentationists. The frictionists taught that the heat of the body was produced by the rubbing of the blood against the walls of the blood vessels, the fermentationists that it was due to fermentative processes going on in the blood.

Black and Lavoisier, about the end of the 18th century, showed that it was caused by **oxidation,** $CO_2$ being the product of the combustion. Lavoisier believed that this oxidation took place in the lungs, but if this were so the lungs would be the hottest organs in the body, and this is not the case. Later it was shifted to the blood stream; but now we know that it takes place neither in the lungs nor in the blood stream but in the tissues themselves.

Oxidation is continually going on in the tissues and this is the source of the heat of the body, just as it is in the case of a candle flame; the difference is that in the one case (body) it proceeds slowly, in the other (candle) more rapidly.

## Body Temperature

Temperature may be measured by a THERMOMETER; this gives the intensity of the heat, but not the quantity of it which is measured by a CALORIMETER.

Animals are divided into two great groups with regard to body temperature, viz.: **warm-blooded** animals and **cold-blooded** animals, the former including mammals and birds, the latter all other animals—reptiles, amphibians, fishes and all invertebrates. Another point of distinction, more important than the actual temper-

ature even, is that the so-called warm-blooded animals have a constant body temperature, and are therefore said to be **homoiothermal,** while the cold-blooded animals have a variable temperature, depending on that of the environment in which they live—**poikilothermal.** A man (homoiothermal) has practically the same body temperature, no matter whether he reside in the tropics or the arctic regions, while a frog or a fish (poikilothermal) takes the temperature of the air or water in which it lives.

HIBERNATING ANIMALS such as the woodchuck, dormouse, bear, etc., form a class by themselves, since during one-half of the year (summer) they are warm-blooded or homoiothermal and during the other half (winter) cold-blooded or poikilothermal.

Clinically the temperature is taken by placing the bulb of the thermometer in the mouth, axilla, or rectum.

The rectal temperature in the human subject varies between 97°F. and 99°F.; muscular exercise may raise it to 102°F. or 103°F., but it quickly subsides during rest. In high fever it may reach 110° F. or over, but 106°F. is serious and 107°F. or 108°F. is dangerous, and if it persists for any length of time, death may result from heat stroke.

The normal body temperature is highest in birds; in the hen it runs from 107°F. to 109°F., and in the humming bird and swallow higher still, viz., 111°F. to 112°F. Most mammals have a higher body temperature than man. In all species it is found to be slightly higher in females than in males.

**Diurnal Variations in Body Temperature**—Man is the most perfect homoiothermal animal but even in him the body temperature is not absolutely constant. If the rectal temperature be recorded every hour throughout the twenty-four, and the results plotted in the form of a curve, it will be found that the temperature is lowest in the early morning, when the subject is asleep, from 2 to 4 A. M., and highest in the late afternoon, when the body is most active. It has a greater range in children than in adults.

## Production of Heat in the Body

The chief seat of heat production is **muscle.** About one-half the total weight of the body is made up of muscle and more than four-fifths of the body heat is produced in muscle. When the muscles are in active contraction, the heat production is greatly increased.

Next to muscle, as a source of heat, come the secreting glands, and of these the **liver** is the most important heat producer. It is doubtful whether the nervous system adds much to the heat of the body, and the metabolism in bone, cartilage and connective tissue is so small that little heat is produced in these tissues, for the amount of heat produced in any tissue or organ is approximately proportionate to the tissue metabolism or oxidation.

### Loss of Heat from the Body

The channels of heat loss are the skin, the respiratory passages and the excreta. Roughly speaking, 80% is lost by the skin, 17% by the air passages and lungs, and 3% by the excreta.

**From the skin** heat is lost, 1, by **radiation, conduction** and **convection,** and 2, by **evaporation of sweat.** If one body is hotter than another, heat will radiate from the former to the latter, and the greater the difference in temperature between the two the more rapidly will radiation take place, and the greater will be the amount of heat lost in a given time. In all habitable climates, with a few occasional exceptions, the temperature of warm-blooded animals is above that of their surroundings, so that heat is constantly being lost from the body by radiation.

In temperate and cold climates animals are provided with a **deposit of fat** under the skin and with **fur** or **feathers,** all of which serve to diminish the loss of heat by **conduction;** in man **clothes** serve the same purpose. The air held in the meshes of the textures of which the clothes are composed, and between the garments, is a more effective protection against the loss of heat than the material of the garments itself, since air is a very poor conductor of heat. When the clothes get wet, the air in the interstices is replaced by water, which is a much better conductor, and this explains, in part, the cooling effect of wet clothes.

A large amount of heat is also lost by **convection.** Even on a still day, particularly in those parts of the body unprotected by clothes, the layer of air in immediate contact with the surface of the body is warmed; it becomes lighter and rises, to be replaced by cold air which, in turn, is warmed and ascends, etc. The heat lost in this way (by convection) is, of course, greatly increased in a draught or on a windy day.

2. **The secretion and evaporation of sweat** is a very important factor in heat loss from the skin. In the evaporation of sweat a large amount of heat is abstracted from the skin and this helps to keep the body temperature below that of its surroundings. Sweat will evaporate most rapidly if the air is dry; if the air is saturated with moisture there will be no evaporation at all. The unclothed human body can stand a temperature of 260°F. for several minutes if the air is quite dry, whereas if it be saturated with moisture, permitting of no loss of heat by evaporation, 89°F. may rapidly cause death. Zuntz records the case of a workman without sweat glands in his skin; during the summer months, when he could lose little heat by radiation, conduction or convection, he was incapacitated for work, since the heat developed from muscular exercise rapidly raised the body temperature to a dangerous point. As long as he kept his shirt wet, however, the temperature remained about normal.

The relative importance of radiation, etc. and evaporation as a means of losing heat depends on the temperature and humidity of the outside air. If the humidity is high, near the saturation point, little heat can be lost by evaporation, and if the external temperature is high little is lost by radiation; if both are high the temperature of the body must rise, since some heat is always being produced in the body, and death may result. **Heat stroke** is easily produced in hot, humid climates and during "heat waves" in summer, in the cities along the Atlantic sea board where the air is often near the point of saturation, hundreds of persons die from this cause.

**Condition of Cutaneous Bloodvessels and Sweat Glands**—The loss of heat from the skin varies with the condition of the cutaneous bloodvessels and sweat glands. If the vessels are DILATED, the skin is warmed by the blood from the deeper parts of the body, and, consequently, MORE HEAT IS LOST by radiation. The coldest blood in the body is found in the cutaneous veins. If the vessels are CONSTRICTED, little warm blood circulates through the skin and LESS HEAT IS LOST. Similarly, when the sweat glands are active more evaporation takes place and more heat is lost, and vice versa.

**From the Lungs and Air-passages** a considerable amount of heat is lost in two ways: 1. The air is inhaled cold and, while in the lungs, is warmed, and the heat absorbed it carries away when exhaled. 2. The evaporation of water from the air passages is also an important factor. In animals, such as the dog, which don't sweat, a large quantity of heat is lost by evaporation from the tongue and air passages.

**The amount of heat lost by the Excreta** is comparatively small. Most foods, including water, are relatively cold when taken into the body and when excreted are warm, but if all the meals be taken hot, heat may be added to the body in this way.

## Regulation of Body Temperature

The temperature of the body will only remain constant so long as the production of heat balances the loss; if more heat is lost from the body than is produced by it the temperature will fall; if more is produced than is lost it will rise. In warm-blooded animals, in health, this balance is maintained by a **heat-regulating mechanism.** The essential difference between a warm-blooded and a cold-blooded animal is that the latter does not possess such a mechanism.

**The Loss of Heat is Regulated both Voluntarily and Involuntarily**—1. **Voluntary Control** is important in man; it is effected by the use of clothes, radiators, fires, etc.

2. **Involuntary Control** comes into play through centers in the nervous system. For example, COLD applied to the skin causes the cutaneous vessels to become CONSTRICTED reflexly through the

vaso-motor center (not directly), thus sending the warm blood from the skin to the deeper parts and diminishing the loss of heat from the skin. WARMTH has the opposite effect; it reflexly DILATES the cutaneous vessels and leads to an increased loss of heat. THE ACTIVITY OF THE SWEAT GLANDS is also under the CONTROL OF THE NERVOUS SYSTEM. Heat applied to the skin stimulates the glands reflexly, through the sweat center, to pour out their secretion which on evaporation causes increased loss of heat. That the sweat glands are excited reflexly through the sweat center, and not directly by the application of heat to the skin, can be proved by cutting the nerve which supplies a certain cutaneous field. After the nerve is divided no amount of heat applied to that field will have any effect on the sweat glands within it; this is because the reflex arcs have been interrupted.

**Heat Production is also Controlled by Voluntary and Involuntary Means**—1. **Voluntary Control** is exercised by increasing or diminishing muscular activity. When cold, we walk or move about; when too warm we rest, thus increasing or diminishing heat production as the case may be.

2. **Involuntary Control** is brought about reflexly through the nervous system. COLD applied to the skin INCREASES MUSCULAR TONUS; at a certain point the contractions become visible—SHIVERING—and more heat is produced. Shivering is involuntary. The bracing effect of a cold climate is due to this increase in muscle tonus. Warm-blooded animals produce more heat as the external temperature falls, while cold-blooded animals produce less.

Since most of the heat of the body is produced in muscle, this would become much warmer than the other tissues if it were not for the BLOODSTREAM WHICH DISTRIBUTES the HEAT and SO equalizes the temperature throughout the body.

**The Effect of Muscular Contraction on Heat Production** can be shown by giving curara to an animal, such as a rabbit, thus immobilizing it; here the body temperature will fall rapidly because no heat is being produced in the muscles. Anæsthesia with ether or chloroform has the same effect, and for this reason the room in which a surgical operation is being performed is always kept very warm.

COLD ALSO STIMULATES THE APPETITE so that more food is consumed, and it is said to induce a desire for fatty foods especially, which have a high heat value. The Eskimo, for example, lives to a large extent, on the subcutaneous fat (blubber) of whales, seals and walruses.

Nervous control is less effective in regulating heat production and heat loss in young than in old animals, and, in consequence, the body temperature is more variable. Newly born animals are very nearly poikilothermal. Thus, fever is not such a serious symptom in a child as it is in an adult, since in the former a com-

paratively slight cause may account for it. Fever, it should be remembered, is only a symptom and not a disease.

Other factors than the influence of the nervous system, which govern the relation between heat production and heat loss, are the following:

1. **Size**—The PRODUCTION of heat is proportional to the MASS or weight of the body and the HEAT LOSS to the SURFACE. The former varies with the cube of the linear dimensions and the latter with the square, so that in small animals the ratio of surface to mass is greater than in large animals, of the same species, hence, weight for weight, more heat must be produced, per unit of body weight, in small animals than in large, to balance the increased heat loss.

2. **The shape** of the animal also influences the ratio between the surface and the mass and hence between the heat loss and the heat production. The sphere offers the smallest surface, per unit of mass, and animals, when they wish to diminish heat loss, roll themslves into a ball; when, on the other hand, it is desirable to increase heat loss they extend the limbs and stretch the body out so as to expose a greater surface.

3. **Age**—Besides the difference in size and shape young animals are growing and are more active than adults and so metabolism and heat production are greater weight for weight, in young than in old animals of the same species.

4. **The degree of obesity** influences the heat loss, to a considerable extent, since the fatty tissue provides a subcutaneous layer of bad conducting material.

## Calorimetry

The temperature of an animal, as indicated by a thermometer, is not a measure of the amount or quantity of heat produced by the animal. To obtain this some form of calorimeter must be used. Animal calorimeters are of two types—the water calorimeter and the air or differential calorimeter.

**The water calorimeter** consists of a double walled metal box, the space between the walls being filled with water. This is placed within a large wooden box and surrounded by such non-conducting materials as shavings, sawdust or felt, to prevent loss of heat from the outside by radiation. The inner box, in which the animal is placed, is provided with an air inflow and outflow tube with a thermometer in each, so that the difference in temperature between the incoming and outgoing air can be determined. Another thermometer is placed in the water jacket, and during the experiment a mixer is kept in motion to ensure that the water is of uniform temperature.

The animal (dog, for example) is placed in the inner box and

allowed to remain there for one hour, say. During this time the heat given off by the animal is communicated to the water, the temperature of which is thus raised. After allowance is made for the heat absorbed by the metal of the box, and by the air in its passage through, the quantity of heat lost by the animal is found by multiplying the weight of water by the increase in temperature. Thus, suppose that the water weighs 30 kilograms and that its temperature is 1.5°C. higher at the end than at the beginning of the experiment, the amount of heat added to the water, that is, given off by the animal is $30 \times 1.5 = 45$ large calories.

Corrections must be made, however, for the possible rise or fall of the body temperature while the animal is in the calorimeter, which is determined by placing a thermometer in the rectum. If the rectal temperature does not change the amount of heat given off by the animal is equal to that produced; if the rectal temperature has risen more heat has been produced than lost, and if the rectal temperature has fallen, vice versa. For example, if the dog weighs 10 kilos and the rectal temperature has risen 0.5°C., $10 \times 0.5 \times 0.8$ (the specific heat of animal tissues) $= 4$ kilocalories, which must be added to the amount lost by the animal; if the rectal temperature has fallen 0.5°C. then the 4 kilocalories must be subtracted. What we desire to determine is the amount of heat produced by the animal in a given time; what we measure directly is the heat lost.

**The Air or Differential Calorimeter** consists of two double chambers, with the air spaces between the walls of exactly the same dimensions, connected to each other by a U-tube containing colored fluid as an index. If the air is warmer in one chamber than in the other the index will move towards the cooler side, and vice versa.

The animal is placed in a wire cage on one side and a HYDROGEN FLAME IS BURNT on the other. The inflow of hydrogen can be regulated by a stop-cock so that the heat produced by the animal is exactly balanced by that produced by the hydrogen flame; when this is so, the index does not move. The amount of heat produced by the flame can be determined from the volume of hydrogen consumed.

**The Bomb Calorimeter** is used for estimating the heat values of food substances. In principle it is the same as the water calorimeter described above. A weighed quantity of the food substance under investigation—butter, starch, white of egg, etc.—usually about 1 gram, is COMPLETELY BURNT IN AN ATMOSPHERE OF OXYGEN when the heat of combustion is communicated to a known weight of water. One gram of fat, burned in this way, will yield 9.3, one gram of carbohydrate (starch) 4.1, and one gram of protein 5.8 large calories.

## EXCRETION

In the general process of nutrition there are three phases to be considered: 1, the bringing of new matter to the tissues in the form of oxygen from the lungs, and the final products of digestion from the alimentary canal; 2, the chemical changes taking place in the tissues, included under the term metabolism; 3, the removal of waste and useless material, the products of metabolism, from the tissues and their elimination from the body. This last is known as **excretion.**

Water and the waste products of body metabolism are thrown off or excreted through four channels, viz.: the liver, lungs, kidneys and skin. It has been shown how the bile constituents are poured into the intestines and partly thrown off, along with the undigested parts of the food which form the fæces, and also how $CO_2$ is eliminated by the lungs, but the excretory functions of the kidneys and the skin still remain to be studied.

## THE KIDNEYS

The kidneys are two in number, right and left; they are situated in the upper part of the lumbar region, one on either side of the middle line, and are surrounded by a large quantity of fat which helps to protect them and keep them in position. The main duct of the kidney is termed the **ureter,** and this conveys the urine (excretion of kidney) to the **urinary bladder,** which serves as a reservoir in which the urine accumulates until it is expelled through the **urethra.** The entrance of the ureters through the wall of the bladder is very oblique and this, as we have already seen in the case of the bile and pancreatic ducts, plays the part of a valve in preventing the urine from a full bladder passing back into the kidneys.

### Structure of Kidney

Each kidney is about 4 inches in length, 2½ inches in width and 1½ inches in thickness, and weighs about 4 ounces. The outer border is rounded and convex, and the inner border concave showing a depression which is termed the **hilum;** it is here that the blood vessels (renal artery and renal vein) enter the organ and the ureter emerges from it. The ureter, at its origin, is spread out into a funnel shaped expansion termed the **pelvis,** and this is further subdivided into smaller funnels termed **calices.** The kidney is dark red in color, and is enclosed in a tough fibrous capsule which is firmly adherent at the pelvis.

On making a **longitudinal section** through the kidney, with a sharp knife, the cut surface is seen, by the naked eye to consist of two distinct parts, an outer or **cortical region** and an inner or **medullary region.** The medullary region is made up of a number of pyramids, lying side by side, with their bases in the cortex all fused together and their apices projecting into the calices of the ureter. They are called the **Malpighian pyramids** and each of them is, in a sense, an independent miniature kidney. The ducts of the uriniferous tubules open on the surface of these pyramids and pour their contents (the urine) into the ureter.

**Bloodvessels of Kidney**—The blood enters the kidney by a single vessel—the **renal artery** which is a branch of the aorta—and leaves it by a single vessel—the **renal vein** which joins the inferior vena cava. The renal artery, on entering at the hilum, divides into branches which run up between the pyramids to which they give off some twigs, and terminate in a complicated system of capillaries in the cortex and medulla. The renal vein and its tributaries take a similar course.

**Uriniferous Tubules**—The kidney is a **compound tubular gland.** Each (uriniferous) tubule begins in the cortex as a cup-like expansion called the **capsule of Bowman** which embraces a tuft of capillaries called the **glomerulus,** the two together forming a **Malpighian corpuscle.** This expanded end narrows into a **neck** as it leaves the glomerulus and then pursues a very devious course, bending back upon itself several times, and forming what is called the **convoluted tubule;** ultimately this tubule ends in one of the **ducts** which open into the pelvis of the kidney. The blood enters the tuft of capillaries (glomerulus) by a single (afferent) vessel and leaves it by a single (efferent) vessel, the latter breaking up into a second set of capillaries which surround the convoluted tubules.

### The Function of the Kidneys

It is the function of the kidney to separate from the blood various substances that are formed elsewhere, as the result of tissue metabolism, and which may be regarded as impurities. This helps to keep the composition of the blood constant. Unlike the other glands which we have previously considered, none of the constituents of the secretion (urine) are formed in the kidney; they are already present in the blood when it reaches the organ, and are simply picked out by the epithelial cells which line the tubules. In the case of some of the constituents of the urine they are practically entirely removed from the blood, by the kidney, urea, for example, almost none being found in the renal vein, whereas in other cases it is only the excess, above a certain limit, that is removed—sodium chloride for example. Many constituents of the blood again, are not touched at all by the healthy kidney,

e. g. the proteins, serum albumin, and serum globulin, etc., and glucose if it is not present in abnormally large quantities. The kidney cells are very senstitive to any change in the composition of the blood and foreign substances, such as drugs, which may be present in minute quantity, are at once thrown out.

**Diuretics** are substances that stimulate the kidney cells to increased activity and so produce an increase in the quantity of urine excreted. Examples are,—CAFFEIN, ALCOHOL, WATER, etc. If water is drunk in large quantities, it is quickly absorbed and dilutes the blood; in this case the excess of water is picked out by the kidney cells and the blood brought back to its normal concentration. One of the hormones found in extracts made from the posterior lobe of the pituitary body acts as a powerful diuretic, but whether it functions in this way normally is not known.

**Nerves of the Kidney**—Both vaso-constrictor and vaso-dilator nerves pass to the kidney, but it is difficult to be certain whether the organ is supplied with secretory nerve fibers and for the following reason: Any circumstance which brings a larger amount of blood to the kidney will lead to an increased activity of the secreting epithelium, producing an increased flow of urine, and similarly, a diminished blood supply will have the opposite effect. If one of the nerves going to the kidney be divided and the peripheral end stimulated, any increase in the secretion of urine which might follow would not necessarily prove that this nerve contained secretory fibers, because the same effect might be produced by the stimulation of vasodilator fibers.

The secretion of urine by the kidney is CONTINUOUS; it passes through the ureters, into the bladder, where it accumulates until the act of micturition takes place.

## Urine

**Human urine** is a yellowish, straw or amber-colored fluid, usually acid in reaction, the acidity being mainly due to acid sodic phosphate. The specific gravity varies from 1015 to 1025, and the quantity passed in 24 hours runs from 1000 c.c. to 2000 c.c. which will contain about 50 grams (1½ ounces) of solids.

**The Composition of Urine** is very complex (see board). It depends to a considerable extent on the quantity and quality of the food. The most abundant constituents are water, urea and sodium chloride. The constituents of the urine may be divided into inorganic and organic substances.

**The inorganic constituents** are chlorides, phosphates and sulphates of sodium, potassium, ammonium, calcium and magnesium, the chief of which is **sodium chloride.**

**The organic constituents** are urea, uric acid, hippuric acid, creatinin, etc., the chief being **urea.** Most of the nitrogen of the

body is excreted in the form of urea, so that the daily amount of this susbstance may be taken as a rough measure of the protein metabolism of the body. One hundred grams of protein, oxidized in the body, yield 33 grams of urea or 16 grams of nitrogen. As we have seen already, much of this is formed in the liver.

There are chemical tests, both qualitative and quantitative, for all the important constituents of the urine. A careful physical and chemical examination of the urine is of great value to the physician in the diagnosis of disease.

When the kidneys fail to act the constituents of the urine are not removed but accumulate in the blood, and this leads to a condition of poisoning known as **"uræmia"** which is rapidly fatal if not relieved.

The abnormal substances most commonly found in the urine in disease, are blood, bile, sugar, albumin and pus.

# SKIN

The skin forms the outer covering of the body, becoming continuous at the various orifices with the mucous membrane which lines the internal cavities.

## Structure of Skin

It is made up of two layers, the **cuticle, epidermis or scarf-skin,** and the **dermis or true skin.** The epidermis, which lies on the surface, consists of stratified squamous epithelium, arranged in several layers. The most superficial layer consists of keratin, a horny substance, which is quite impervious to water. The epidermis is pierced by the ducts of the sweat glands and by the hairs, where these are present, but it contains no blood vessels so that bleeding does not take place when the cuticle is cut or shaved off, until the true skin is reached. It is thickest on the palms of the hands and the soles of the feet.

**The dermis or true skin** forms the chief part of the bodily covering. It is composed of fibrous tissue, dense in the part next to the epidermis, looser deeper down, near the subcutaneous fat; it is very vascular and contains the terminal organs of the sensory fibers of the skin. It passes insensibly into the areolar, subcutaneous tissue which contains numerous groups of fat cells. The superficial layer of the dermis is raised up into projections called papillæ, on which the epidermis is moulded, and this prevents the latter from being easily separated or rubbed off. The root of the hair in its follicle lies in the true skin, and its stem or shaft penetrates the epidermis obliquely. A small muscle consisting of non-striped fibers is attached to each hair follicle so that when it contracts the hair is erected or set on end. It is called the **arrector pili** muscle.

**Glands of the Skin**—These are of two varieties—the sebaceous and the sweat glands.

**The Sebaceous Glands** are small, saccular glands the ducts of which open into the hair follicles. They are lined by epithelial cells, and the sebaceous material secreted by these is poured into the hair follicles and serves to lubricate the roots of the hairs and the skin.

**The Sweat Glands** are found over the whole skin, but they are especially numerous on the palms of the hand and the soles of the feet. They consist of very long, simple tubules, the deeper or secretory portion being coiled up in the dermis, with the duct piercing the epidermis and opening on to the surface. The sweat is secreted by the epithelial cells that line the deeper part of the

tubule and escapes through the duct, spreading over the surface of the skin. It has been estimated that there are two million sweat glands in the skin, over the whole body.

The mammary glands are modified sweat glands which secrete milk instead of sweat.

### Secretion of Sweat

The amount of sweat secreted in the 24 hours varies greatly from day to day, depending upon outside temperature and muscular exercise mainly, and no definite figure can be given, but probably it is safe to say that, on an average, as much water is eliminated by the skin as by the kidneys. When the sweat is produced in small quantity it evaporates rapidly, and never becomes visible on the surface; this is known as **insensible perspiration.** When it is secreted more rapidly, and there is not sufficient time for it to be completely evaporated, it gathers as droplets on the skin and this is known as **sensible perspiration.** If the air is warm, dry, and in constant motion, much sweat will be evaporated without ever becoming visible. The amount of sweat discharged on the skin, other things being equal, will be inversely proportional to the quantity of urine secreted by the kidney.

Animals differ greatly in the amount of sweat which they secrete. The horse sweats very freely over the whole body, while the dog and cat have no glands except on the pads of the feet, and rabbits, rats, mice and goats are said not to sweat at all. In man the skin practically all over the body perspires, but is more active in some regions, such as the palms of the hands, the soles of the feet and the skin of the forehead, than in others.

**Influence of Nervous System on Secretion of Sweat**—The secretion of sweat is a **reflex phenomenon** and is under the control of the nervous system, as we have seen when discussing heat regulation. This can be proved by the following experiment: The cat, when exposed to a warm atmosphere, sweats freely from the pads of the feet. If the sciatic nerve be divided in a cat and the peripheral end stimulated, a copious secretion of sweat will appear on the pad of the corresponding foot. When the wound heals in this animal, if it be placed in a warm room sweat will be formed on the pad of the sound hind limb but none on the side where the nerve has been cut. This proves that the application of HEAT TO THE SKIN HAS NO DIRECT EFFECT ON THE SWEAT GLANDS.

**The sweat center** is situated in the medulla oblongata, and can be acted on reflexly from the periphery or from the higher centers in the cerebrum. Strong emotion, such as fear, may stimulate the sweat center and cause the "cold sweat to break out."

**Sudorifics**—Certain drugs which increase the secretion of sweat are called sudorifics. Some of these appear to act on the sweat

center and others on the terminations of the secretory nerves in the glands. Of the latter, **pilocarpin** is the best example, while **atropin** has the opposite effect, paralyzing the secretory fibers. Camphor and ammonium acetate stimulate the sweat center.

**Composition of Sweat**—It is very difficult to obtain pure sweat for chemical analysis because it is mixed with the secretion from the sebaceous glands, usually. It is a thin, watery fluid, of low specific gravity (1004) and contains only very small quantities of solids. The most abundant are sodium chloride and urea, but normally these are present in little more than traces. $CO_2$ may also be found, but in very minute quantities; sweat in health is practically pure water. In disease, where the kidneys are not functioning properly, a considerable amount of urea, and also of the other constituents of the urine, may be found in the sweat. Under these conditions, the skin appears to be able to act vicariously for the kidney, to a considerable extent.

## Functions of the Skin

The following functions belong to the skin:

1. It forms a PROTECTIVE and SENSITIVE covering for the body.
2. It REGULATES BODY TEMPERATURE through the blood supply and the secretion of sweat.
3. To only a slight extent in health, but to a considerable extent in kidney disease, it serves to ELIMINATE WASTE PRODUCTS from the body.
4. In mammals it PROVIDES NUTRIMENT FOR THE OFF-SPRING, since in the female, the mammae are modified sweat glands.
5. In thin, moist skinned animals, such as the amphibia, a large amount of RESPIRATORY EXCHANGE takes place through the skin.

## THE ENDOCRINE ORGANS OR GLANDS OF INTERNAL SECRETION

The glands so far considered, discharge their secretions through a duct on to a free surface; these might be called **external secretions.** Other glands, still to be studied, manufacture secretions which do not escape through a duct but pass directly, or through the lymphatics, into the blood vessels. These are termed **internal secretions** and the organs which produce them, **glands of internal secretion** or **Endocrine Organs.** The study of these glands, their secretions and the effects of them on the body form the science of **Endocrinology.**

Many of these have no ducts and are termed **ductless glands;** others, such as the pancreas and pituitary, produce both external and internal secretions and are accordingly provided with ducts.

These internal secretions belong to the group of substances termed **hormones** which are believed to act in the body as **chemical co-ordinating agents.** This method of correlating the activities of organs was originally the only method, before the evolution of a nervous system, and still persists, even in the higher animals, where rapidity of action is not required. When the activity of one organ A, is to excite another organ B, the activity of B may be evoked, either by a nerve impulse, passing from A to the central nervous system and from this to B (**reflex action**) or by a special chemical substance, produced at A and carried in the bloodstream to B (**hormone action**).

The following is a list of the glandular structures in the body that are believed to produce internal secretions. Some have ducts and others are ductless.

### Glands of Internal Secretion

| | |
|---|---|
| Suprarenals | Ductless Glands. |
| Thyroid | |
| Parathyroids | |
| Pineal Body? | |
| Ovaries | |

Pyloric glands of stomach
Duodenal glands
Pancreas
Pituitary
Testes

## SUPRARENAL CAPSULES OR ADRENAL GLANDS

In man, one of these glands lies on the upper end of each kidney, forming a sort of capsule, hence the name **suprarenal gland** or **capsule;** in most other animals they are situated near the kidney, and so are termed **adrenal glands.**

### Structure

The gland is surrounded by a connective tissue CAPSULE which sends in SEPTA between the columns of cells of which the organ is composed. When sectioned it is seen to consist of an **outer cortex,** yellowish in color, and an inner **medullary portion** in the center. The cortex is composed of epithelial cells, that are arranged in radial columns which are supported by strands of connective tissue, in which lie many capillaries. The cells of the medulla form an irregular network; they are granular and often pigmented, and they contain a substance which is stained brown by the salts of chromic acid. This is called **chromaffine** substance on account of its affinity for stains or dyes.

The cortex and the medulla have a different origin developmentally, the former coming from the mesoderm, the latter from the ectoderm. They are also believed to have distinct and separate functions. In the elasmobranch fishes the two exist as separate organs, and are not associated anatomically in the way they are in mammals, the cortex being represented by the interrenal body and the medulla by the paired bodies which lie near the ganglia of the sympathetic chain.

### Functions of Suprarenal Glands

The glands of internal secretion are not infrequently diseased in man, and much of our knowledge of their functions has been derived from a study of the symptoms arising under these conditions. In investigating the functions of these glands generally, we may study 1, the effects of non-development or disease in man; 2, the effects of their removal in animals, and 3, the effects of extracts, made from the glands, when injected into other animals or their administration to man as therapeutic agents. We shall follow this order in the case of the suprarenal glands.

In the physiology of the adrenals there are four epoch-making discoveries which may be considered.—1, the relation of the destruction of suprarenals to a group of symptoms first observed by Addison in 1855; 2, the fact that intravenous injection of an extract of the medulla causes a very marked rise in blood pressure discovered by Oliver and Schafer in 1894; 3, a third very important addition to our knowledge of the subject was made in 1902 when Takamine succeeded in isolating this pressor substance and preparing it in the

pure crystalline form; 4, and a fourth important generalization was made when it was shown that all the various actions of the pure secretion, adrenaline, are due to is stimulation of the nerve endings of the sympathetic nervous system.

1. **Effects of Disease in Man**—The physician Addison of London, in 1855, first pointed out that destruction of the supra-renal capsules, by tubercular disease, led to a train of symptoms of which the following are the chief: (a) **General muscular weakness** and prostration, with frequently **low blood pressure**; (b) **pigmentation of the skin**; (c) attacks of **vomiting.** The condition, almost invariably, ends fatally. It is now known as **Addison's disease.** It is a rare disease, and usually attacks young adults, being more common in men than in women. There is feeble heart action, loss of appetite, disturbances of the digestive tract and other symptoms which can be accounted for by loss of the normal stimulation of the peripheral endings of the sympathetic nervous system.

The most striking feature of the disease is the pigmentation of the skin which may represent anything from a slight bronzing to the dark hue of a negro. Microscopically the pigment is found in the deepest cells of the epidermis. The cause of this pigmentation is not known.

The excessive muscular weakness is always pronounced in Addison's disease. The patient is always tired without any apparent cause. The condition is almost invariably fatal.

2. **Effects of Removal**—In animals, when the whole gland is removed, on both sides, **death follows** in from two to four days.

3. **Effects of Injection of Extracts of the Gland**—A watery extract of the whole gland, when injected into the vein of an anæsthetized animal, **raises the general blood pressure** markedly. The same effect is obtained from an extract of the medulla alone, and this is due to the fact that the medullary portion contains a hormone, which excites the nerve endings in the non-striped muscle of the arterioles, thereby causing their constriction. With both vagi intact the heart rate is slowed, probably a reflex effect through the depressor nerve fibers caused by the high blood pressure.

When the vagi are cut across and all nerve connections destroyed the heart beats faster and more powerfully showing that on the heart muscle itself the action of adrenaline is favorable. It has the specific property of stimulating the nerve terminations of the sympathetic system everywhere.

Cannon has shown that intravenous injection of adrenalin causes an increase in blood sugar. Stimulation of the nerves of the adrenals have the same effect and this is believed to explain the increase of sugar in the blood, which follows emotional excitement. The hyperglycemia may lead to glycusoria and this temporary or

emotional glycusoria has been observed in students after examination and in the spectators at athletic contests. In this case the adrenaline may act on the sympathetic end-organs in the liver so as rapidly to transform the glycogen stored in the liver into sugar.

Whether adrenaline acts on striated muscle has not been proven. The beneficial effect on muscular power which appears to follow adrenaline administration when studied by means of the ergograph may be due to the increased amount of sugar set free in the circulation.

It is said that adrenaline shortens the time of blood coagulation. If this is so it is the only effect which cannot be explained as the result of sympathetic stimulation.

It is probably the diminished quantity or absence of this hormone which leads to the low blood pressure and muscular weakness in Addison's disease.

This hormone was isolated by Takamine and is called **adrenalin.** It is a comparatively simple substance, chemically, and has been synthetized in the laboratory and prepared artificially in this way. It has the following formula: $C_6H_3(OH)_2.CH\,OH.CH_2.NH_2.CH_3$ and is chemically known as dioxy-phenyl-ethanol-methylamin. It is used extensively in medicine to stop hæmorrhage, because it has a powerful constrictor action on blood vessels. This substance is being produced continuously in small quantity, by the medulla of the suprarenal capsule, passed into the blood, and carried to the tissues where it probably helps to maintain the tonus of the bloodvessels.

**The Function of the Cortex** is not known. It is difficult to investigate, in mammals, because it cannot be removed without, at the same time, injuring or interfering with the blood supply of the medulla. Injection of its extract produces no effect at all, nevertheless, it is believed that the CORTEX IS ESSENTIAL TO LIFE, for, when this part is removed in fishes, where it exists as a separate organ, and can be taken away, without damaging the medullary tissue, death follows, whereas, if the medullary portion alone is removed, it leads to no bad effects.

There is some evidence of a relationship between the cortex and the generative organs but the real nature of this is unknown. Castration is said to cause hypertrophy of the adrenal cortex in male animals. The chemical composition of the adrenal cortex shows a large quantity of phosphorus-containing lipoids which by some are held to be very significant.

## THYROID GLAND

The thyroid gland lies in the neck and, in the human subject, it consists of **two lobes,** a right and a left, situated one at each side

of the upper part of the trachea, and united across the middle line by a narrow **isthmus.** In many animals the isthmus is represented by little more than a few strands of connective tissue so that the thyroid may be regarded as bilateral.

### Structure

It is surrounded by a connective tissue capsule and consists of a framework of connective tissue, enclosing a large number of small **saccules or vesicles.** Each vesicle is lined by a single layer of **cubical epithelium** and contains a translucent, viscid material termed **colloid.** This colloid substance is believed to be secreted by the epithelial cells lining the vesicles and to contain the active principle of the gland, a substance rich in iodine and named thyroidin first isolated by Kendall. The gland is very vascular.

### The function of the Thyroid Gland

This, as in the case of all the other glands of internal secretion, was for a long time an enigma, but these organs were not considered to be of much importance to the body. Wharton (1656) states that the thyroid gland has four functions: "1, The first and principal use of these glands appears to be to take up certain superfluous moistures from the recurrent nerve and to bring them back again, into the vascular system, by their own lymph channels. 2, To cherish the cartilages to which they are fixed which are rather of a chilly nature by their own heat. 3, To conduce by their exhalations to the lubrication of the larynx and so to render the voice smoother, more melodious and sweeter. 4, They contribute much to the rounded contour and beauty of the neck; for they fill up the empty spaces about the larynx and make its protuberant parts almost to subside and become smooth, especially in the female sex, to whom, on this account, a larger gland has been assigned, which renders their necks more even and beautiful."

### Diseases associated with Abnormal Conditions of the Thyroid Gland

There are three diseases, in the human subject, the cause of which is believed to be some abnormal state of the thyroid gland, viz.: Myxœdema and cretinism, due to absence or diminished secretion of the specific hormone which it produces, and exophthalmic goitre or Grave's disease, due to over secretion. The first two are included under the general term **hypothyroidism** and the last under the term **hyperthyroidism.**

**Myxœdema** (Gull's disease) is a condition that appears in adults, most frequently in women. The symptoms are: 1, overgrowth of the subcutaneous connective tissue, leading to swelling of the skin or **œdema,** particularly of the hands and face; 2, **slow heart beat**—

the rate may be down to 40 per minute, 3, **mental dulness;** the patient, who used to be bright and active, becomes slow and clumsy in mind and body. There is a general depression of all the functions accompanied by a lowered bodily metabolism, almost always associated with a condition of mental depression. The thyroid gland may be enlarged (goitre), but if this is the case, it is not a true overgrowth of the essential gland tissue but is due to a hypertrophy of the connective tissue frame work, leading to an obliteration of many of the vesicles and a corresponding diminution in the secreting power of the gland.

The above symptoms, if not remedied, will **result in death,** which may take place only after some years, however. They disappear rapidly when the essential substance is supplied by administering to the patient the thyroid gland (or its extract) of one of the lower animals such as the sheep or pig. When this treatment is stopped the symptoms appear again, because the tissues are deprived of the active substance present in the gland. A very small quantity (a few milligrams) of thyroxine administered daily will have the same beneficial effect as the gland itself, or its extract.

**Cretinism** is the same condition, in the child, as myxœdema in the adult, resulting from defective thyroid secretion—a condition of **hypothyroidism.** The gland may be absent at birth, or under developed, or diseased. The child, in such a case, remains **dwarfed and undeveloped in mind and body;** at thirty it is a stunted, pot-bellied creature with the intelligence of a child of four or five years. The treatment is the same as for myxœdema, viz.: the administration of the proper quantity of sheep's or pig's thyroid or thyroxine and it must be kept up throughout life, as in the case of the adult.

Iodine is a very important constituent of the thyroid hormone, thyroxine, and in regions where it is deficient in the drinking water the addition of small quantities of potassium or sodium iodide are believed to be useful in counteracting the effects of hypothyroid conditions.

**Exophthalmic Goitre** or **Grave's Disease**—This condition is believed to be due to **excessive thyroid secretion.** The cardinal symptoms are just the opposite of those of myxœdema, viz.: 1, **goitre,** or swelling of the thyroid gland; 2, **exophthalmos** or protrusion of the eyeballs; 3, **rapid heart action**—the rate may be 120, or over, per minute; 4, **muscular tremors and excessive nervousness.** The same symptoms may be induced in normal individuals by the administration of thyroid extract, leading to the presence in the body of an excess of the active substance. There is a great increase in oxidation in the body as indicated by observations on the basal metabolism, a condition the reverse of what is found in hypothyroidism.

THE TREATMENT here indicated is removal of part of the thyroid, in order to lessen the secretion or tying off some of the blood-vessels supplying the gland. If all the gland be removed, however, myxœdema will follow. Grave's disease is usually fatal if not treated in time.

**Extirpation of the Thyroid Gland in animals** leads to **cretinism** or **myxœdema,** according to the age of the animal, while the administration of the gland, or of its extract, by mouth or subcutaneously, produces symptoms of exophthalmic goitre.

**Function of the Thyroid Gland**—Judging from the facts related above, the function of the thyroid gland would appear to be to produce an internal secretion (hormone), in this case thyroxine—a substance rich in iodin—which is essential for the proper growth and functional activity of the tissues, particularly those of the nervous system.

It has a profound effect on growth and development. The metamorphosis of tadpoles and of salamander larvæ into adult forms are greatly influenced by thyroid feeding. Tadpoles which receive small amounts of thyroid in their food are quickly transformed into very small frogs, while those which have the thyroids removed by operation do not metamorphose but grow into large tadpoles.

It has an important effect on the skin and its appendages. In thyroidectomized sheep and goats the wool and hair fall out and horn growth is greatly retarded.

## PARATHYROID GLANDS

**The parathyroids** are small glands, as a rule four in number, situated somewhere in relation to the thyroid. There are usually two pairs,—an **internal** pair and an **external** pair. In the **herbivora** the internal pair are imbedded in the substance of the thyroid while the **external pair lie outside,** usually at some distance from the gland. In the **carnivora both pairs** are either **imbedded in the substance of the gland** or lie within its capsule.

**In Structure** the parathyroid is unlike the thyroid. It consists of elongated and irregular columns of granular epithelial cells, held together by strands of connective tissue extending from the surrounding capsule. The cells do not form vesicles as in the thyroid. The gland has a very rich blood supply.

It is not certain whether any specific disease in the human subject results from pathological changes in the parathyroids, but many believe that the condition known as **tetany** or "convulsions," sometimes seen in children, is caused by a deficiency in parathyroid secretion. The connection is not so certain, however, as that between cretinism and the thyroid, for example.

**Extirpation of all the parathyroids in animals** leads to acute muscular **tetany,** with **high temperature** (the result of severe muscular contraction) and **rapid breathing.** Death follows within a few days. Similar symptoms have been observed in a few cases, in the human subject, where the surgeon has accidentally removed the parathyroids along with the thyroids.

Feeding with parathyroid tissue, or the administration of calcium salts, is said to relieve the symptoms both in the human subject and in animals, but parathyroid transplantation is most effective.

**Function of the Parathyroids**—According to some these glands are believed to secrete a substance which is essential for the proper metabolism of **calcium** in the body. The muscular tetany, resulting from the removal of the parathyroids, is said to be caused by the diminished quantity of calcium in the brain. The substance or hormone, secreted by the glands, has not been isolated as it has in the case of adrenalin and thyrocine.

The latest theory of parathyroid function, advanced by Noël Paton, is that this gland removes from the circulation certain toxic substances produced in normal protein metabolism, viz.: guanidine and methylguanidine. If these are allowed to accumulate, as happens when the parathyroids are absent or diseased, intoxication indicated by mucular spasms and other symptoms follow which usually ends fatally.

The following facts are advanced in favor of this view—1. The eating of protein foods aggravates the symptoms in para-thyroidectomized dogs and hastens death. 2. When salts of guanidine are injected into the veins of normal animals tetanic convulsions follow. 3. In dogs from which the parathyroids have been removed guanidine and methylguanidine are found in excessive quantity in the blood. 4. A frog's nerve-muscle preparation placed in blood drawn from a dog from which the parathyroids have been removed will show tetanic twitchings.

## PINEAL BODY OR GLAND

This is a small body of a reddish color, found in the upper part of the brain, between the two cerebral hemispheres. It has the structure of a secreting gland, with cells of epithelial origin, connective tissue framework, etc., but little is known regarding its function.

In children, disease of this organ, leading to its destruction, is held by some to be followed by the early onset of puberty, with great sexual and mental precocity, and early death. If this is so, the internal secretion produced by the pineal gland, might be regarded as having an inhibitory influence on the development of the sexual organs.

Whether the pineal gland should be included amongst the endocrine organs may be regarded as an open question.

## GENERATIVE GLANDS OR GONADS

Besides their generative functions, these organs (ovaries and testes) are believed to produce internal secretions which have a beneficial effect on the general body metabolism, especially of the nervous system. **Castration** in both sexes is followed by **obesity,** and **dulled mentality.** When a young male animal (deer or sheep for example) is **castrated,** the **secondary sexual characters,** such as the appearance of horns in the deer or sheep, or the growth of a beard in man, **do not develop,** nor does the sexual appetite appear at the age of puberty. If the duct, through which the spermatic fluid (external secretion of testes) escapes be tied, on both sides, no such results follow however. This would appear to prove that an internal secretion is produced in the interstitial cells of the testes which normally promotes the growth of the secondary sexual characters,—horns, beard, etc.

Steinach tied the spermatic duct on both sides and after some months he reported an increase in sexual instinct and in general vigor. His explanation is that the cells of the seminiferous tubules degenerate while the interstitial tissue undergoes hypertrophy accompanied by an increased production of sex hormone.

When the ovaries are removed from young animals the growth of the uterus is arrested and in the human subject menstruation does not begin, or, if the operation is performed after sexual maturity, it ceases.

## PYLORIC AND DUODENAL GLANDS

The glands at the pyloric end of the stomach and those of the duodenum, which produce as internal secretions the hormones **gastrin** and **secretin** respectively, have already been considered under digestion. To the one (gastrin) the term "hormone" was first applied, and the other (secretin) was the first of the group of hormones to be discovered.

## PANCREAS

This, like the testes, pyloric and duodenal glands, is a gland with both an internal and an external secretion, the latter having been taken up in the study of digestion in the small intestine.

**Removal of the Pancreas in Animals** is followed by the appearance of sugar in the urine, which is secreted by the kidney in excessive amount; abnormal thirst and hunger, with emaciation and

death in from two to four weeks. Practically the same symptoms are present in the disease known as **diabetes mellitus in man.**

That these results are not due to the want of the external secretion (pancreatic juice) is proved as follows:

1. If, instead of removing the gland, the **duct** is **ligatured** or blocked with solid paraffin, thus preventing the entrance of the external secretion into the duodenum, **glycosuria** (sugar in the urine) and the other symptoms, do not appear.

2. If a portion of the pancreas, after removal from the abdominal cavity**,** is **grafted** under the skin or in muscle, no symptoms follow.

In these two cases the connection with the duodenum is completely cut off, so that none of the pancreatic juice can be available for digestion, and yet no symptoms follow. This proves that the cause of the symptoms, when the pancreas is removed, is not want of the pancreatic juice.

On the basis of experiments such as the above, it is believed that the pancreas forms an internal secretion which plays an important part in **carbohydrate metabolism.**

**Islets of Langerhans**—These have been mentioned in the general description of the pancreas given under digestion. They consist of islands composed of granular epithelial cells, belonging to the secretory type, with a rich blood supply, and showing no connection with the secreting tubules of the gland which produce the external secretion. There is considerable evidence to show that the internal secretion of the pancreas comes from these islets of Langerhans; they show pathological changes in cases of diabetes mellitus in man.

**Functions of the Internal Secretion of the Pancreas**—Several theories have been put forward to explain the action of this internal secretion. 1. Its presence in the portal circulation may be necessary to enable the liver cells (a) to **transform sugar into glycogen,** or (b) to **check the too rapid retransformation of glycogen into sugar.** (See Glycogenic Function of Liver, p. 119). 2. It may be required by the tissues, particularly muscle, to enable them to **utilize the sugar** circulating in the blood. On any one of these theories, absence of the secretion or hormone, would lead to **hyperglycæmia** (excess of sugar in the blood) and **glycosuria** (presence of sugar in the urine).

Since the secretion is effective after boiling, the active substance is a hormone and not a ferment. It has not been isolated, so far.

We have seen that in the case of thyroid deficiency the administration of thyroid substance or of the hormone thyroxine in the proper quantity cured the condition for the time being. This would seem to indicate that similar treatment, viz.: the administration of pancreatic substance containing its active principle, would have some beneficial influence on diabetes mellitus. This has been tried

but without success. Recently the reason why seems to have been given by Banting and Best. These experimenters ligatured the ducts of the pancreas in the dog, allowing the animal to live for some weeks. On removing the pancreas at the end of that time it was found that the acinar cells producing the external secretion had become atrophied but not the islets of Langerhans. On injecting an extract of this degenerated pancreas into a dog suffering from diabetes it was found that the sugar disappeared from the urine at once. The apparent cause of the ineffectiveness of an extract of the normal pancreas is that the enzymes of the pancreatic juice, notably the trypsin, destroy the sugar regulating hormone believed to be secreted by the islets of Langerhands and now termed **insulin.** McLeod and his co-workers have shown that active insulin may be obtained from the normal pancreas if it be treated with mineral acid sufficiently concentrated to destroy the digestive enzymes immediately after the animal is killed.

Insulin is now being used extensively in the treatment of diabetes in man. Very small quantities of it quickly lower the blood sugar but only for some hours after administration so that it is not a cure. In order to keep the blood sugar to the normal limit so that none shall appear in the urine insulin must be injected subcutaneously once or twice daily.

By giving too much insulin the blood sugar in normal animals may be reduced to such an extent that convulsions follow which may end in death unless the effect be counteracted by injecting glucose.

## PITUITARY BODY OR HYPOPHYSIS CEREBRI

The so-called pituitary body is a composite organ consisting of two lobes, a **glandular lobe** and a **nervous lobe.** It is attached to the base of the brain by a slender stalk (stalk of pituitary) and lies in a small cavity, in the sphenoid bone, termed the sella turcica (Turkish saddle).

Embryologically the two parts are quite distinct. The large anterior or glandular lobe is derived from the epithelium of the mouth cavity, while the smaller posterior or nervous lobe is developed from the brain. Part of the glandular lobe surrounds, almost completely, the nervous portion and this is termed the **pars intermedia;** it consists of epithelium and is included in the posterior lobe.

**Acromegaly**—Hypertrophy of the anterior lobe in man gives rise to the condition known as **acromegaly** in which there is a great overgrowth of bone in particular, and other changes that, after a variable time, prove fatal.

**Giantism** or **Gigantism**—If the hypertrophy of the gland takes

place before the epiphyses have united, a great increase in the development of the long bones results and the individual becomes a giant in stature the condition being known as **gigantism.** If the disease does not develop until after ossification is complete the effects are most evident in the thickening of the long bones, particularly at the extremities. There may be some lengthening of the spinal column leading to kyphosis (curvature of the spine) but not to an increase in stature. The bones of the face enlarge, particularly the lower jaw. An early symptom is failure of the sexual power. This condition is termed acromegaly as distinguished from gigantism.

**Removal of the whole gland,** in animals, was believed to be fatal in a few days, as also removal of the anterior lobe alone, while the taking away of the posterior lobe alone leads to no ill effects. Recent work would seem to show that in dogs complete removal is not always fatal. The animals show a general tendency to put on fat and the reproductive glands undergo degeneration.

Removal of the pituitary in young dogs causes dwarfing to a marked degree, associated with obesity and a low degree of intelligence. Basal metabolism is decreased and in many respects the condition resembles that due to removal of the thyroids.

**Injection of extracts of the posterior lobe** intravenously, in an anæsthetized animal, is followed by: 1, a rise in the blood pressure; 2, increased flow of urine; 3, secretion of milk in lactating animals. In this case, however, there does not appear to be a real increase in the secretion of milk but rather a more effective emptying of the gland by stimulation of plain muscle. There is no increase in the quantity of milk yielded in the twenty-four hours.

While posterior lobe extract stimulates plain muscle generally it appears to have a special action on the parturient uterus and on this account is extensively used in midwifery.

It has a very pronounced action on the kidney leading to a remarkable increase in the amount of urine excreted.

**Injection of extracts of the anterior lobe** produces no evident effects at all, and yet, it is the anterior lobe which is essential to life, while the physiologically active posterior lobe is not.

The excretion from the posterior lobe, or a part of it, is external and is poured into the third ventricle of the brain, where it mixes with the cerebro-spinal fluid; the secretion of the anterior lobe is internal and passes directly into the blood vessels.

**Functions of the Posterior Lobe**—It produces a hormone (or hormones) which, 1, helps to maintain the **tonus of non-striped muscle;** 2, stimulates the **kidney** to secrete urine; 3, stimulates the **mammary gland** to secrete milk. It may be that a single substance brings about all these different effects, or, which is more

probable, that there are three distinct hormones furnished by the posterior lobe.

**Functions of the Anterior Lobe**—This lobe is believed to produce one or more hormones which are connected with the processes of growth, particularly of the skeleton. A substance **tethelin** has been prepared from the anterior lobe which is said to produce an increase in growth in young animals to which it is fed. Its chemical constitution has not been determined.

Much is still unknown regarding the physiology of the pituitary gland.

## LIVER AND KIDNEY

The term "internal secretion" was first applied by Claude Bernard in relation to the liver. He designated bile the "external secretion" and, in contradistinction, the glycogen formed in the liver and absorbed as sugar into the bloodvessels the "internal secretion." This, however, is not a hormone and is not now regarded as a true internal secretion.

It is reported by some investigators that a true internal secretion is produced in the **kidney** which helps to maintain the tonus of the blood vessels, but this statement needs confirmation.

**The Spleen** is a ductless gland but there is no evidence that it produces an internal secretion. It is not essential to life, since it may be entirely removed in animals without any permanent ill effects. In fœtal life and early infancy it is believed to manufacture red blood corpuscles, and probably also in adults, after severe hæmorrhage.

## THE SENSES

**The Sensory Mechanism** consists of 1, peripheral end organs or **receptors;** 2, a **chain of neurons** for the transmission of the impulses arising in the receptors; 3, **sensory centers** in the brain where the impulses arrive and make their impression.

The receptors are subdivided into three groups, 1, those that are situated on the outer surface of the body, termed the **exteroceptors;** 2, those in the alimentary canal and viscera, the **enteroceptors;** 3, those found in the muscles, tendons and joints, and in the semicircular canals of the ear, the **proprioceptors.**

**Adequate Stimulus**—The end organ of each sense has its own specific stimulus; e. g. the retina is excited by light waves but not by sound; the hair cells of Corti, in the cochlea of the ear, by sound waves and not by light, etc. This is known as the ADEQUATE STIMULUS; light is the adequate stimulus for the eye, sound for the ear, pressure for certain end organs in the skin, etc.

**Law of Specific Nerve Energy**—Stimulation of the end organs belonging to any one of the senses gives rise to the sensation peculiar to that sense, e. g. ethereal waves, of a certain wave length, falling on the retina, give rise to the sensation of sight, but the same sensation is aroused when the retina is excited mechanically, as, for example, by applying pressure to the eyeball, or by using an electrical stimulus. This is known as MULLER'S LAW OF SPECIFIC NERVE ENERGY"

**Threshold Stimulus**—For each sense a certain minimal strength of stimulus is necessary to produce the sensation, and this is called the LIMINAL OR THRESHOLD STIMULUS. This will vary in different individuals, and, from time to time, in the same individual, depending on the excitability of the end organ. Fatigue, for example, will raise the threshold value and rest will lower it. The phenomenon of SUMMATION is seen in sensation, as in reflex action, where a series of subminimal stimuli, applied in succession, will reach the threshold value and produce an effect.

**Weber's Law**—The increase of stimulation necessary to produce the smallest perceptible change in a sensation is proportional to the strength of the stimulus already acting. For example, if a weight of 30 grams be held in the hand, an extra half gram added will produce no perceptible difference, but one gram will; if the original weight is 60 grams then to make a perceptible increase in the sensation 2 grams must be added. Similarly, if a room is illuminated with 100 candles one more candle added will make a perceptible difference in the illumination, but if there be 1000

candles, 9 additional candles will make no difference; 10 will be required, that is 1/100th of the original stimulus. This is known as WEBER'S LAW. It is only true within certain limits, however.

One drawback in the study of sensory phenomena is the want of a unit by which the end reaction may be measured. In the motor nerve we have the muscle which reacts, or the action current, and both can be measured quantitatively, but the end reaction for a sensory nerve is a state of consciousness for which we have no standard of measurement.

## CUTANEOUS SENSATIONS

The sensations derived from the skin are those of pressure of various kinds, heat, cold, pain. The end organs representing these different sensations have not been made out with certainty, but it is known that there are localised areas or spots on the skin which, when stimulated, give rise to different sensations.

**Warm, Cold, Pressure and Pain Spots**—If a blunt pointed wire be cooled in ice, and then drawn slowly over the back of the hand, every now and again it will come on a spot where it is felt to be cold; these spots are termed "cold spots" and can be marked with ink; they do not shift their position. If now the wire be heated, and the operation repeated, a number of spots will be found which give a sensation of warmth. These may also be marked with ink; they do not coincide with the cold spots. Similarly, by using the prick of a needle as the stimulus, a series of pain spots may be located, and lastly spots that respond to pressure alone.

EACH OF THESE SPOTS GIVES RISE TO ITS OWN SPECIFIC SENSATION. For example, any stimulus, applied to a warm spot, that will excite it, such as electricity, gives rise to a sensation of warmth, and similarly for the others. Menthol applied to the skin appears to stimulate the cold spots alone, and so feels cool, while carbon dioxide gas, when the arm is immersed in it, excites the warm spots only, giving rise to a warm sensation.

It is found that the pain spots are most numerous; next in order come the pressure spots, then the cold spots and lastly the warm spots which are fewest in number.

All nerve fibers conveying impulses from the sense organs of the skin enter the spinal cord through the posterior roots of the spinal nerves, and the brain through the corresponding parts of the cranial nerves, and pass up, over a series of neurons, to reach the center for cutaneous sensibility in the cerebrum, which is believed to be situated in the region of the Rolandic fissure.

## SENSE OF TASTE

The senses of taste and smell are closely associated, and it is not always possible to discriminate betwen them. Their end organs are excited by chemical substances, either in solution (taste) or in the form of vapor (smell).

The terminations of the nerves of taste are situated, for the most part, in the tongue, but the soft palate, the uvula and the upper part of the pharynx also possess them to some extent. The **posterior third** of the tongue, as well as the parts just mentioned, is supplied by the **glosso-pharyngeal** nerve and the **anterior two-thirds** by the **chorda tympani.** These are the nerves of taste.

### Taste Bulbs

The mucous membrane of the posterior part of the tongue especially, show epithelial structures termed taste bulbs, which are most numerous in the walls of the circumvallate papillæ, but they are also present in the other papillæ and over the general surface. Each taste bulb contains two kinds of cells—the **gustatory cells,** the ends of which project into the pore of the taste bulb, and surrounding these the **supporting cells** which form a sort of envelope for the gustatory cells.

### Taste Sensations

There are four primary taste sensations—SWEET, BITTER, ACID, SALT. In order to stimulate the gustatory cells around which the terminal fibers of the taste nerves end, the substance to be tasted must be in solution; if placed on the tongue dry, no taste sensation is felt, until it is dissolved in the saliva. Possibly each of these primary taste sensations has its specific sense organ, since they are found to be more or less localised in the different regions of the tongue surface. Sweet tastes are felt especially at the tip and sides of the tongue, while bitter tastes come from the back part and also from the soft palate and pharynx. Salts stimulate the tip of the tongue and acids the sides. Chewing the leaves of a certain plant—GYMNEMA SYLVESTRE—abolishes the sensations of sweet and bitter while those of acid and saline are unaffected and also tactile sense. Cocaine, on the other hand, paralyses the tactile sense sooner than the sense of taste. This would appear to show that the end organs in the tongue are specific for these sensations.

The peripheral organs of taste and smell are so closely related that many of the flavors obtained from substances, introduced into the mouth, are really simultaneous sensations of taste and smell.

**Fatigue**—If a sapid substance is kept in the mouth for some time, or tasted repeatedly, the taste becomes less and less distinct, and this would appear to be due to fatigue in some part of the taste

mechanism. If a sufficient interval is allowed to elapse, the sensation is fully appreciated again.

It must be remembered that the tongue in addition to taste possesses also tactile sensibility.

## SENSE OF SMELL

### End-organs

The end-organs for the sense of smell are distributed over the mucous membrane of the upper part of the nasal cavities. The olfactory mucous membrane, as it is called, is covered by epithelial cells which are of two kinds—the olfactory cells and the supporting cells. The olfactory cells are long and slender each with a large nucleus. Each is a bipolar cell with two processes one of which passes to the free surface and ends in a bundle of fibrils resembling cilia which show no movement however, while the other penetrates the cribriform plate of the ethmoid bone and forms a synapse with a mitral cell of the olfactory bulb. The supporting cells are of the long columnar type; they are set closely side by side so as to give support to the sensory cells.

The afferent nerve fibers of the sense of smell lie in the first pair of cranial nerves—the **olfactory**—and the impulses from the nasal mucous membrane, after passing over several neurons, reach the center for smell in the cerebrum which is believed to be situated near the taste center in the uncinate gyrus.

The smelling mechanism is much more highly developed in some animals—the dog for example, than it is in man and it plays a much more important part in the lives of these animals; a dog recognizes his friends or his enemies more certainly by the sense of smell than by sight.

### Sensations of Smell

In order to stimulate the olfactory cells the substance must be in the form of gas or vapor; when liquids are poured into the nose they do not give rise to any odor. No satisfactory classification of odors has yet been arrived at such as we have seen in the sense of taste. They may be divided roughly into pleasant and unpleasant odors.

The sense of smell is much more delicate than the sense of taste. The odor of musk can be detected when the substance has been diluted with air eight million times, and mercaptan in a dilution of one in twenty-five billions. The smelling mechanism is easily fatigued; the sensation obtained from a perfume decreases rapidly when inhaled for a considerable time, and people sitting in a badly ventilated room very quickly get accustomed to the disagreeable odor which is felt at once by a person entering from the fresh air.

Some individuals have no sense of smell at all while in others it is partially absent; they perceive certain odors but are insensible to others.

## SENSE OF HEARING

### Peripheral End-organs

The peripheral organs in the sense of hearing are found in the cochlea in the inner ear. They consist of modified epithelial cells termed the **hair cells of Corti**; the hairs from their free ends project into a fluid, the endolymph, and catch up the sound vibrations which are transmitted to that fluid from the tympanic membrane. These cells translate the sound vibrations into nerve impulses which are carried by the auditory or 8th cranial nerve to the hearing center, situated in the temporal lobe of the cerebrum. The outer and middle ears are merely mechanical devices for transmitting the sound waves to the inner ear.

The Organ of Hearing is divided into three parts—the outer ear, the middle ear or tympanum and the inner ear.

### Outer Ear

The outer ear consists of the PINNA or **auricle** lying outside the skull and the **external auditory meatus,** a canal leading down to the tympanic membrane. The auricle is mobile, being provided with two sets of muscles in some of the lower animals, the horse for example, and serves to collect the sound waves, but in the human subject mobility is not essential, since the head can be so easily turned round. In man it is of little service as a sound collector, because if filled up with wax, the central opening being left patent, the hearing is not perceptibly changed.

**The external auditory meatus** is about 1¼ or 1 inch long. It follows a curved course, forwards, inwards and slightly upwards with the concavity downwards; it is narrowest about the middle so that if an object gets pushed in beyond this point it is difficult to remove. It is lined by skin, with hairs and ceruminous glands in the outer half only. These glands are of the simple tubular type, like the sweat glands, and they secrete a bitter, oily substance, the cerumen or ear wax, which protects the lining of the canal from drying and helps to deter insects from entering.

### Middle Ear or Tympanum

The middle ear or tympanum consists of an irregular cavity in the temporal bone; it is flattened from side to side, and contains air, the tympanic ossicles, two muscles, and a nerve—the chorda tympani. The cavity communicates with the throat through a long duct, the Eustachian tube. The outer wall of the tympanum communicates with the external auditory meatus, the opening

between the two, in the recent state, being closed by a membrane—the **tympanic membrane** or drum of the ear. On the inner wall of the tympanum there are two openings, the fenestra ovalis and fenestra rotunda. The former leads into the vestibule of the inner ear and is closed by the foot of the stapes, while the latter is closed by a membrane which separates the cochlea from the tympanum. The higher of the two is the **fenestra ovalis,** leading in to the vestibule of the inner ear; it is closed by the foot of the stapes and the orbicular ligament. The other opening is the **fenestra rotunda** which communicates with the cochlea and is also closed by a membrane. Sound waves are transmitted by the chain of ossicles and reach the inner ear through the fenestra ovalis.

In birds the transmitting mechanism is very simple; it consists of a single rod of bone, called the COLUMELLA, which extends from the tympanic membrane to the fenestra ovalis. By this arrangement the effect of the sound waves, on the comparatively large tympanic membrane, is concentrated on the much smaller fenestra ovalis.

**Tympanic Ossicles**—Stretching across the cavity of the middle ear is a chain of three small bones—the tympanic ossicles—named the malleus (hammer), the incus (anvil) and the stapes (stirrup). These small bones are articulated together in such a way that any movement of the tympanic membrane to which the handle of the malleus is attached is transmitted to the inner ear by the stapes, the incus lying between the malleus and stapes and articulating with both.

These small bones form a series of levers by the action of which the movements of the tympanic membrane, caused by the sound waves entering through the external auditory meatus, are concentrated on the much smaller fenestra ovalis and transmitted to the perilymph of the inner ear with increased force.

**Muscles of Middle Ear**—These are two in number, the tensor tympani and the stapedius muscles.

**The tensor tympani muscle** arises from the cartilage of the Eustachian tube and is inserted into the handle of the malleus. When this muscle contracts, the handle of the malleus is pulled inwards and one idea is that this helps to lock the inco-malleal joint more firmly, so that feeble vibrations are transmitted more perfectly. It is believed that this muscle is used when we strain to hear faint sounds. It is supplied by a small branch of the 5th nerve. When sound waves enter one ear the tensor tympani on both sides can be observed to contract, the reflex traveling through the motor center of the 5th nerve.

**The stapedius** is inserted into the neck of the stapes. It is supplied by a branch of the 7th nerve. The function of this muscle is not certain; some say that its contraction by twisting the foot

of the stapes in the fenestra ovalis leads to a tightening of the orbicular ligament and so to a damping of the vibrations the muscle being used to protect the inner ear from the effects of loud sounds.

**The Eustachian Tube** extends from the tympanic cavity to the throat. It is a canal of about 14 inches long consisting partly of bone and partly of cartilage, and its function is to allow of the equalization of the air pressure inside and outside the tympanic membrane. When this tube is inflamed and occluded, dulness of hearing results. The explanation is that the oxygen of the air, in the now closed tympanic cavity, is absorbed by the blood and the nitrogen alone is left; the pressure inside becomes less and less and the tympanic membrane bulges inwards and is stretched thus preventing its vibrating so well to the sound waves. Normally it is kept closed but is opened periodically by the act of swallowing.

## Inner Ear

The inner ear is an irregularly shaped cavity in the temporal bone. It is divided into the osseous and the membranous labyrinths, which lie one within the other.

**The osseous labyrinth** is divided into three parts—the VESTIBULE in the middle, into which the sound waves are transmitted, the SEMICIRCULAR CANALS posteriorly and the COCHLEA anteriorly. The whole bony cavity is lined by periosteum, and internal to this is a fluid—the PERILYMPH. Inside the osseous labyrinth lies the membraneous labyrinth which consists of a series of sacs and ducts filled with a fluid termed the endolymph.

**The membranous labyrinth** is the essential part of the ear. The vestibule contains two membranous sacs called the **utricle** and the **saccule;** the former communicates with the three membranous semicircular canals, and the saccule communicates with the canal of the cochlea and with the utricle.

**The Cochlea**—The human cochlea is a tube, wound spirally two and one-half times around a central stem called the **modiolus** through which runs the fibers of the auditory nerve. From the modiolus there projects a spiral lamina of bone a little more than half across the cochlear canal, the **osseous spiral lamina.** It resembles a spiral staircase. From the free margin of the osseous spiral lamina a membrane passes across to the periosteum of the outer wall; this is named the **basilar membrane** and it divides the bony canal into two divisions, one towards the apex and another towards the base. On the apical side of this membrane is placed another termed the **membrane of Reissner,** and in this way the whole tube is divided into three canals or scalæ. The **scala tympani** lies nearest the base; it is so named because, if followed downwards, it opens into the tympanum through the FENESTRA ROTUNDA which is closed by a membrane. The **scala vestibuli** lies nearest the apex,

and at its lower end is the FENESTRA OVALIS, closed by the foot of the stapes and the orbicular ligament. The **scala media** forms the middle division; it is also known as the **cochlear canal** and it forms the cochlear division of the membranous labyrinth.

The scala vestibuli and scala tympani communicate with each other at the apex of the cochlea through a round opening called the **helicotrema.** The perilymph in the vestibular canal can flow through this opening into the tympanic canal and escape by the aqueduct of the cochlea. The cochlear canal contains ENDOLYMPH and each of the others PERILYMPH.

## Minute Structure of Cochlea

The basilar membrane increases in breadth from the base to the apex of the cochlea. In man it consists of a single layer of connective tissue fibers running parallel to each other and stretching across from the osseous spiral lamina to the periosteum of the other side like a suspension bridge. On the apical side of this bridge is placed the organ of Corti.

**The Organ of Corti**— This is formed of several kinds of epithelial cells. The **rods of Corti** are modified epithelial cells and are arranged in two rows— an inner row and an outer row—which meet together at the top, like the rafters of a house. They are planted on the basilar membrane, to which each is connected by a broad foot, and form a tunnel called the CANAL OF CORTI.

A second set of supporting cells are the **cells of Deiters.** These also are modified, epithelial cells, planted by broad bases on the basilar membrane. The hair cells of Corti sit on the shoulders of Deiter's cells.

**Hair Cells of Corti**—On the inner side of the rods of Corti each of these cells is supported on the shoulder of a Deiter's cell and is cemented to it by a granular substance; the lower extremity is prolonged into a stiff cuticular process which is attached to the basilar membrane. They are arranged in rows along the whole length of the cochlea; one row lies internal to the pillars of Corti and, in man, four or five rows external to them. Each is an elongated, epithelial cell with a deeply placed nucleus and granular protoplasm around it. From the free extremity there project a number of short, stiff, hair-like processes which pass only a little way into the protoplasm; their free ends stick out, through one of the apertures in the cuticular lamina, into the endolymph. The fibers of the auditory nerve end around the deeper extremities of the hair cells as terminal arborisations. There are no bloodvessels in the organ of Corti. It is nourished by the endolymph in the scala media. It is believed that these hair cells form the apparatus by which the sound waves entering the ear give rise to the nerve

impulses which are carried by the fibers of the auditory nerve to the center for hearing in the brain.

The **membrana tectoria,** or membrane of Corti, is placed immediately above the hair cells. It is a soft, structure which lies like a pad over the organ of Corti. This membrane is possibly thrown into vibration by the sound waves, thus causing the hairs of the hair cells to indent the protoplasm of the cells and so excite them. On the other hand, some believe that the membrana tectoria acts as a damper, to check the movements of the hairs after the sound vibrations in the endolymph have ceased.

**Cochlear Division of the 8th Nerve**—The bipolar cells from which the fibers of the cochlear nerve arise are found in the SPIRAL GANGLION which is situated within the bone in the base of the osseous spiral lamina. One branch passes to the hair cells, the other into the modiolus and thence to the brain.

**Course of Sound Waves**—Sound waves consist of longitudinal vibrations of the air molecules giving alternate phases of condensation and rarefaction. In the phase of condensation of the sound wave the tympanic membrane is pushed inwards and this, through the series of ossicles, pushes in the foot of the stapes which communicates its movement to the perilymph, and the condensation wave enters the vestibular canal through the fenestra ovalis. From the scala vestibuli it passes through Reissner's membrane into the scala media, reaching the hairs of the hair cells through the membrana tectoria, causing them to indent the protoplasm of the cells and so give rise to nerve impulses. Then it passes onwards, through the basilar membrane, into the perilymph of the scala tympani, bulging out the membrane that closes this canal at the fenestra rotunda. In the phase of rarefaction the movements are in the opposite direction. For musical sounds these waves may vary from seventy feet to a fraction of an inch.

## Sound Sensation

The auditory sense excels all others in its power of distinguishing different qualities of sensation; it can distinguish tones varying in frequency from 16 per second to 40,000 per second, that is through a range of 11½ octaves. It also excels all other senses in its power of analysing tones and picking out their component parts. It is certain that the cochlea is the part of the ear that enables us to perceive musical sounds. How is this brought about?

There are SEVERAL THEORIES OF HEARING but only two will be mentioned here. 1, Helmholtz's resonance theory and 2, Rutherford's telephone theory.

**Helmholtz's Resonance Hypothesis**—This depends on the principle of SYMPATHETIC VIBRATION. If one sound a note of a particular pitch, in a room containing a piano with the dampers raised,

the string of the piano, which is tuned to give that note, will immediately respond; if a note of a different pitch is sounded, another string will respond, etc. In the cochlea, according to Helmholtz, a similar mechanism exists. When a certain note is sounded the appropriate fiber of the basilar membrane is thrown into vibration, and so causes the stimulation of the hair cells planted on it. A note of a different pitch will set another fiber of the basilar membrane vibrating which will stimulate another set of hair cells and give rise to a different sensation, etc. If two tones are sounded together, the two corresponding fibers of the basilar membrane will respond, and so an analysis of the compound sound wave, which enters the ear, will be effected in the cochlea. According to this theory there are, within the organ of Corti, vibrating structures that respond specifically to all the notes within the range of hearing and these structures are claimed to be the fibers of the basilar membrane. These fibers range from 0.041 mm. to 0.495 mm. in length, the shortest ones being found at the base of the cochlea and the longest ones at the apex, so that it is probably the width of the basilar membrane that determines the tuning to any particular note.

**Rutherford's Telephone Hypothesis**—According to this theory, all the fibers of the basilar membrane and all the hair cells vibrate to notes of every pitch, just as the plate of a telephone receiver reproduces the pattern of the vibrations falling on the transmitter. Each note sets up a different pattern of nerve vibration so to speak, and gives rise to a different sensation in the cerebrum. The analysis is made, not in the cochlea, but in the cerebrum.

While there are certain facts difficult to explain by either of these hypotheses the former appears to be most satisfactory to the majority of physiologists.

**The range of hearing** for musical tones extends from notes of 16 vibrations to 40,000 vibrations per second, but when the vibrational frequency is very high the sensation produced is painful. Galton's whistle can give out notes from 6,000 to 80,000 per second, but any above 40,000 cannot be perceived and the highest notes heard are very irritating.

The **acuteness of hearing** is measured by the distance from the ear at which a watch can be heard ticking.

The direction from which a sound is coming is judged of by turning the head around until the position is found at which the sound is heard loudest.

Sound can be transmitted not only through the outer and middle ears but THROUGH THE BONES OF THE HEAD. If the sound of a small tuning fork be allowed to die away until it can no longer be heard, and then the handle applied to the teeth of the lower jaw or to the top of the head, it can be heard again distinctly. This is

because the sound is better conducted through the bones of the skull than through the air.

**Subjective sound sensations** are caused by excitation of the auditory center in the brain other than by the entrance of sound waves into the ear. The ordinary "singing in the ears" is not a subjective sensation; it is probably due to spasm of the tensor tympani or stapedius muscle in the middle ear.

### Semicircular Canals

The Semicircular Canals have no relation to the sense of hearing. Stimulation of the cells lining these canals produce rotatory movements of the head, and their function is to enable us to maintain our equilibrium in space. They may be called the peripheral organs of the sense of equilibrium. This, along with the muscular sense, belongs to the proprioceptive system.

## SENSE OF SIGHT

The eye is the organ of sight. It is constructed on the principle of the camera obscura or photographic camera. It consists of a series of lenses for the purpose of focusing the images of objects on the retina, which corresponds to the sensitive plate of the camera.

### Structure of Eye

The eyeball consists of three coats surrounding the transparent media which serve as lenses for the formation of images.

**Corneo-sclerotic Coat**—The outer covering is formed by the **sclerotic coat** or white of the eye which becomes continuous in front with the transparent cornea. It is composed of dense, fibrous tissue, mainly, and its function is protective. In front the fibers lie parallel to each other, and this arrangement allows of the transmission of light, whereas the sclerotic is opaque. This transparent part is the **cornea;** it has a somewhat greater convexity than the sclera; it is covered in front by stratified squamous epithelium, while its posterior surface is lined by a single layer of squamous epithelium. The radial fibers of the ciliary muscle take their origin from the corneo-sclerotic junction.

**The conjunctiva** is a connective tissue membrane, with a superficial layer of stratified squamous epithelium, which covers the front of the sclerotic coat and is reflected on to the posterior surface of the eyelids. It is represented on the cornea only by the layer of stratified squamous epithelium.

The **Middle Coat** consists of the **choroid** prolonged forwards as the ciliary processes and the iris. It is very vascular and contains a great number of pigment cells. The choroid lines the sclerotic coat on the inside to within a short distance of the corneo-sclerotic

junction; it is continued forwards, from that point, as the **ciliary processes,** about seventy in number, which consist of connective tissue with pigment cells and bloodvessels. They also contain the **ciliary muscle** which is composed of non-striped fibers, and consists of a radial portion and a circular portion. The radial fibers arise at the junction of the cornea and sclerotic and are inserted into the ciliary processes and neighboring part of choroid. The circular fibers lie inside the radial fibers.

**The iris** is that part of the choroid which extends in front of the lens. It consists of fine, fibrous tissue, with many blood capillaries and pigment cells. This gives the color to the eye; in dark eyed people the pigment is abundant while in blue eyes it is less abundant. The circular opening in the iris is the **pupil** of the eye. Besides the delicate connective tissue, it contains two sets of plain muscle fibers. One set is circular and forms the **sphincter pupillæ** muscle, because when its fibers contract the pupil becomes smaller or is constricted; the other set consists of radiating fibers and forms the **dilator pupillæ** muscle, since the contraction of its fibers produces a widening or dilatation of the pupil.

## The Retina

The retina forms the **inner coat** of the eyeball. It extends forwards to the roots of the ciliary processes. It is a delicate, semi-transparent membrane and consists of the following eight layers from without inwards.

1. The layer of pigment cells.
2. The layer of rods and cones.
3. The outer nuclear layer.
4. The outer molecular layer.
5. The inner nuclear layer.
6. The inner molecular layer.
7. The layer of ganglionic nerve cells.
8. The layer of nerve fibers.

These various layers are held together by the fibers of Müller. Essentially the retina consists of three sets of superimposed neurons, extending from the layer of rods and cones inwards to the layer of nerve fibers.

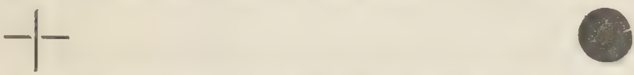
The sensitive elements of the retina are the **rods and cones;** these are the structures that are stimulated by light and give origin to the nerve impulses which reach the vision center, in the occipital lobe, through the fibers of the optic nerves. The rods are much more numerous than the cones over the general surface of the retina but at a certain spot—the fovea centralis—only cones are present. Each rod and cone has an outer and an inner segment. The outer segment of the rod contains a purple or violet pigment while the inner segment is clear; both are rod-shaped. In the cone the

outer segment is colorless and conical in shape while the inner segment is bulbous. From the inner segments of both rods and cones long slender processes pass inwards, each with an expanded portion corresponding to a nucleus. The outer nuclear layer consists mainly of the nuclei of the rods and cones.

The outer layer of the retina really belongs to the choroid. It consists of **hexagonal pigment cells** which send down processes between the rods and cones. These processes are believed to act as sheaths for the rods and cones and to absorb the light which has escaped them. When light falls on the retina the pigment granules stream down the processes between the rods and cones and when the light stimulation ceases the pigment moves back again.

**Optic Disc or Blind Spot**—The retina is deficient at the point where the optic nerve enters and this spot is blind; there are only nerve fibers here and no visual cells. It is placed about 1/10th inch internal to the optic axis, i. e. the antero-posterior axis of the eyeball. When the eye is examined with the ophthalmoscope the entrance of the optic nerve is seen as a whitish disc, the whiteness being due to the presence of a medullary sheath in the nerve fibers. The central artery and vein of the retina radiate from it.

**Marriotte's Experiment**—That there is a blind spot in the retina can be proved by the following experiment: Make two marks, a dot and a cross, on the paper as below, about 3 inches apart; look at the cross with the right eye, keeping the left eye closed, and hold the book about 10 inches from the eye, when both dot and cross will be seen. Now gradually bring the paper towards the eye; at a certain distance the dot will disappear, but on bringing the book still nearer the dot will appear again. It disappears when its image falls on the optic disc or blind spot. (See diagram.)



**The Yellow Spot,** so called because yellow pigment is found in the retina in this region, is that part of the retina where vision is most acute. It is only about 2 mm. in transverse diameter and about 1 mm. in vertical diameter. There is a depression in the center of this area called the **fovea centralis** and here the layers of the retina, internal to the visual cells, are very thin. At the fovea centralis only cones are present, while in the marginal region of the yellow spot there are also rods, but the cones are more numerous. As we pass from the center to the periphery of the retina the cones become fewer and the rods more numerous. There are no large bloodvessels, only capillaries, at the fovea centralis.

By **Clerk Maxwell's Experiment** one may see the **yellow spot** or **macula lutea** in one's own eye. Place a solution of CHROME ALUM

in a glass vessel with parallel walls and look through it at a window; a purplish-red, irregularly circular disc will appear in the field of vision and this will be a projection of the yellow spot. The chrome alum solution transmits red and greenish-blue rays to the retina; the yellow pigment of the macula lutea absorbs the greenish-blue rays and allows the red rays only to reach the cones, so that a purplish-red image, corresponding to the outline of the yellow spot, is projected into the field. This experiment proves that the yellow pigment lies between the sensitive cells of the retina and the source of light.

**The blood vessels of the retina** all come from the central artery of the retina, which enters the eyeball in the optic nerve, about its center. They spread all over the retina, in its inner layers, and can be distinctly seen with the ophthalmoscope. That the blood vessels of the retina also lie between the visual cells and the crystalline lens through which the light enters is proved by

**Purkinjes' Experiment**—In a darkened room, with a sheet of grey paper on the wall, illuminate the inside of the eye by holding a taper at one side, so that the light enters through the sclerotic coat and not through the cornea; a number of branching figures, like the roots of a tree, will be seen on the paper. On moving the taper backwards and forwards the figures also move. These figures are caused by the shadows of the bloodvessels falling on the sensitive elements of the retina. These shadows are always being cast on the sensitive cells and projected into the field of vision, but it is only when the light enters from an unusual direction, and they are thrown on parts of the retina unaccustomed to them, that we are conscious of them.

The yellow spot is placed in the visual axis and lies a little external to the center of the retina through which the optic axis passes. Vision is most acute at the fovea centralis. When we look at the page of a book only those letters the images of which fall on the fovea centralis are sharply defined.

## Vitreous Humor

The vitreous humor is a jelly-like mass filling the larger portion of the interior of the eyeball, and lies behind the crystalline lens; it is enclosed in a transparent envelope called the hyaloid membrane which separates it from the retina.

## Crystalline Lens

The crystalline lens is enclosed in a thin, colorless, homogeneous **capsule** which is very tough and difficult to rupture. The lens is not attached to the capsule and readily slips out when the latter is cut through. It is perfectly transparent and colorless throughout the greater part of life. It is biconvex, the posterior surface

being more convex than the anterior, and the density increases from without inwards. It is composed of fibers, arranged in concentric layers like those of an onion; the fibers are denticulated or notched at the edges, the notches interlocking so as to keep them accurately in position and allow of no lateral movement. The shape of the lens changes with age. In the fœtus it is nearly spherical and as age advances it grows flatter. About 50 it begins to lose its elasticity and becomes denser, these changes being progressive.

**Suspensory Ligament**—The crystalline lens, inside its capsule, is retained in position by the suspensory ligament. At the margin of the lens this ligament divides into two layers, comparatively short, and continued only a little way over the surface of the capsule to which they are firmly cemented by a colorless material. If the eye of an ox be removed from the head of a recently killed animal, and kept for 8 or 10 days, this cement substance decomposes, and the lens within its capsule can easily be shaken free. The suspensory ligament is derived from the hyaloid membrane which encloses the vitreous humor; at the outer end it is attached to the ciliary processes of the choroid coat. When the ciliary muscle is relaxed the suspensory ligament is on the stretch, and being attached to the capsule of the lens, it pulls on the lens and keeps it flattened so that, when the eye is at rest, that is, while the ciliary muscle is not contracting, the eye is accommodated for distant vision. When the ciliary muscle contracts it pulls forward the choroid and ciliary processes; this relaxes the suspensory ligament and the crystalline lens, in virtue of its elasticity, bulges and becomes more convex; in this way the eye becomes accommodated for near vision.

The space between the anterior surface of the lens and the cornea is filled with a watery fluid termed the **aqueous humor.**

## The Eye considered as an Optical Instrument

Parallel rays of light are brought to a focus, by a convex lens, at a point called the **principal focus** of the lens, and the distance between this point and the lens is the **principal focal distance.** There is, therefore, only one principal focus for each lens, but many **secondary foci.** The rays proceeding from a luminous point, placed at the principal focus, are not brought to a focus at all by the lens but emerge from it as parallel rays. For the FORMATION OF AN IMAGE, the object must be placed OUTSIDE THE PRINCIPAL FOCUS (see diagrams). If the object is placed at twice the focal distance of a biconvex lens the image is formed at twice the focal distance, and these two points are termed **conjugate foci.** If the object be placed farther away than twice the focal distance, the image will be smaller than the object, and if it be placed within

twice the focal distance, between that and the principal focus, the image will be larger than the object. All the images produced on the retina are SMALLER THAN THE OBJECTS seen and are **inverted.**

The position of the principal focus of a lens, that is, its focal distance depends 1, on the CURVATURE OF THE LENS; the greater the curvature the shorter is the focal distance; and 2, on the REFRACTIVE INDEX of the substance of which the lens is composed; the higher the refactive index the shorter is the focal distance

In the normal eye the retina is in the principal focus of its lenses. This means that parallel rays of light are brought to a focus on the retina without any action of the ciliary muscle; no effort is felt when the lens is accommodated for a distant object.

While the refractive media of the eye are the cornea, the aqueous humor, the crystalline lens and the vitreous humor, there are virtually only **two lenses** in the eye; the cornea and the aqueous humor together act as a single lens and the crystalline lens is the other. The three refracting (and reflecting) surfaces are the ANTERIOR SURFACE OF THE CORNEA, the ANTERIOR SURFACE OF THE LENS and the POSTERIOR SURFACE OF THE LENS. At the posterior surface of the cornea there is no refraction because the refractive indices of the cornea and of the aqueous humor are practically the same, so that the two together form one lens.

## Accommodation of Eye for Near and Distant Objects

Some adjustment of the eye is necessary in order to see near and distant objects with the same system of lenses, since the eye cannot at the same time focus both parallel and divergent rays on the retina. The adjustment is effected entirely by the crystalline lens and this may be brought about in two ways—1, BY VARYING THE DISTANCE BETWEEN THE LENS AND THE RETINA, and 2, BY ALTERING THE CURVATURE OF THE LENS. The former method is that adopted in the photographic camera, where the lens is moved backwards and forwards, until the image is brought to a focus on the ground glass plate. This is also the method used in certain fishes, where the lens is moved backwards or forwards by a special muscle; but in man, and the higher mammals, the second method is the one employed, viz.: that of changing the curvature of the lens. The lens is rendered more convex to focus near objects on the retina and less convex for distant objects. The means by which these changes in the curvature of the lens are brought about is termed the

**Mechanism of Accommodation**—As mentioned previously, in the normal eye, looking at a distant object, the crystalline lens is flattened by the tension on the suspensory ligament. When it is desired to look at a NEAR OBJECT the CILIARY MUSCLE CONTRACTS, pulls forwards the ciliary processes, to which the suspensory liga-

ment is attached, and so RELAXES THIS LIGAMENT. This removes the tension from the lens, which BECAUSE IT IS ELASTIC bulges or becomes more convex, and so the image which, in the resting state of the eye fell behind the retina, is now brought forwards until it falls on the retina. Accommodation is fatiguing because it requires muscular action; when we read a book the ciliary muscle is always in action.

The anterior surface of the lens bulges more in accommodation than the posterior surface; in fact the latter hardly changes its curvature at all. This is known by a study of

**Sanson's Images**—If a candle be held at one side of a person's eye an observer, looking in the eye, will see THREE IMAGES of the candle flame—one by reflection from the ANTERIOR SURFACE OF THE CORNEA, one from the ANTERIOR SURFACE and another from the POSTERIOR SURFACE OF THE LENS. The first is the brightest; the second is larger and dimmer than the first but, like it, erect; the third is small and so dim that it is difficult to detect, and it is INVERTED because it is reflected from the posterior surface of the lens which acts like a concave mirror. These are termed **Sanson's images.** When the candle is moved images 1 and 2 move in the same direction as the candle but image 3 moves in the opposite direction.

Now ask the subject to look first at a distant and then at a near object, and watch the changes that take place in the sizes and relative positions of the images. No change occurs in the first image but the second image becomes smaller and somewhat brighter when the person looks at a near object, and at the same time approaches the first. The reduction in size of the second image shows that the surface from which it is reflected (anterior surface of lens), has increased its curvature, and the increase in brightness of the second image, and its approach to the first, proves that the anterior surface of the lens comes nearer to the cornea. The third image, like the first, shows practically no change, either in brightness or position, and this shows that the surfaces from which the first and third images are reflected, viz.: anterior surface of cornea and posterior surface of lens, do not change during accommodation.

By means of an instrument termed the PHAKOSCOPE Sanson's images may also be seen, but the simple experiment, just described, demonstrates them quite as effectively.

**Changes in Pupil during Accommodation**—During accommodation the pupil undergoes changes in size; when the eye looks at a NEAR OBJECT it DIMINISHES IN SIZE, when it looks at a DISTANT OBJECT the pupil INCREASES IN SIZE. The mechanism by which this is brought about will be described under "Functions of the Iris," but the object is to diminish spherical aberration.

**Spherical Aberration** is a defect of the optical apparatus. Rays

of light passing through the circumference of a lens are more bent than those passing through the center, therefore they are not focused at the same point, and the image is blurred. In an optical instrument, such as a telescope or microscope, this defect is corrected by using a DIAPHRAGM to cut out the peripheral rays. In the eye this method is also adopted; the iris cuts out the peripheral rays. The image of an object will be most distinct and best defined when the pupil is smallest, but it must not be too small so that enough light is not admitted. When we look at a near object it is desirable to have a well defined and distinct image.

**Chromatic Aberration** is another defect of the optical apparatus. This is due to the fact that when white light is refracted or bent it is also dispersed; the red rays are less bent than the violet rays and the result is an image surrounded by a colored ring. In optical instruments this is corrected by using TWO LENSES OF DIFFERENT MATERIAL in combination such as crown glass and flint glass; this gives an achromatic system. In the eye this optical defect is remedied in a similar way, to some extent, viz.: by admitting the light through a combination of lenses.

**Range of Accommodation. Near and Far Points of Vision**—In every eye there is a limit to the power of accomodation. If a book be brought nearer and nearer to the eye, at last a point is reached beyond which the type can't be seen distinctly. This is the **near point of vision.** It varies with age; in the adult it is usually about 6 inches but in the child it is only about 3 inches.

**The near point of vision** may be determined as follows: With a needle pierce two holes through a piece of paper or cardboard so that both shall fall within the diameter of the pupil.

Hold the paper in front of one eye, closing the other, and look at the needle held in front through the holes. Move the needle backwards and forwards, nearer and farther from the eye. When held at a distance greater than about 6 inches a single needle will be seen but on bringing it nearer, it will appear to be doubled and slightly blurred. The distance at which the needle ceases to appear single is the near point of vision for that eye.

When the needle is nearer than this the lens cannot be rendered sufficiently biconvex to focus the two pencils of light on the retina and the result is two blurred images instead of one sharp and clear.

**The far point of vision** theoretically is at an infinite distance from the eye, if the object is large enough. Practically, however, it is found that rays proceeding from a point 20 to 30 feet distant are sufficiently parallel to be focused on the retina without accommodation. Any object nearer than 20 to 30 feet in the normal eye to be seen clearly requires the use of the ciliary muscle. The normal range of vision then is from infinity to the near point distant from the eye about six inches.

### Common Defects of Vision

Defects of vision occur when the image is imperfectly focused on the retina.

**Emmetropia** is the term applied to normal vision; parallel rays are brought to a focus on the retina without active accommodation. Any defect in the refractive surfaces or shape of eyeball renders the eye ametropic.

**Presbyopia**—At the age of about 50 years for most individuals the elasticity of the lens perceptibly diminishes so that it does not become so convex as formerly on contraction of the ciliary muscle during accommodation. The object to be seen sharply must be held at a greater distance from the eye and this is known as presbyopia or the long-sightedness of age. It is corrected by wearing converging spectacles.

**Hypermetropia** is another form of long-sightedness. It is most frequently caused by abnormal shortening of the eyeball so that parallel rays are focused behind the retina, and it is usually congenital, the eyeball from birth being smaller than the normal. When a distant object is looked at a clear image can only be obtained when the eye is being accommodated so that the ciliary muscle is always in action. A hypermetropic eye can never be rested. When the muscle is paralyzed by atropine no object can be seen clearly. To prevent this constant strain converging spectacles must always be worn.

**Myopia or Short-Sightedness** is exactly the reverse of hypermetropia; parallel rays are brought to a focus before reaching the retina. The cause is usually an elongation of the eyeball, but it may be due to an increased curvature of the refracting surfaces. This defect may be congenital but it is usually acquired. The remedy is diverging glasses to throw the image back to the retina. It is usually DUE TO AN ELONGATION OF THE EYEBALL ANTERO-POSTERIORLY, so that parallel rays are brought to a focus in front of the retina, but it may be caused by an increased curvature of the cornea. The REMEDY is biconcave or plano-concave lenses so as to render the RAYS OF LIGHT DIVERGENT before they enter the eye.

**Astigmatism**—This defect, which is present to some extent in almost all eyes, is due to IRREGULARITY IN THE CURVATURES OF THE DIFFERENT REFRACTIVE MEDIA OF THE EYE, usually the cornea, but sometimes the lens. Thus, the eye may be short-sighted in the vertical direction and long-sighted for all rays entering horizontally, or vice versa, so that all the lines radiating from a center cannot be focused sharply at the same time. This condition is corrected

by astigmatic lenses of curvature similar to that of the abnormal eye but reversed.

### Functions of the Iris

1. It serves to diminish spherical aberration, as we have already seen, but cutting off the peripheral rays, and 2, it regulates reflexly the amount of light that enters the eye.

The iris contains two muscles which are antagonistic in their action, viz.: the **sphincter pupillæ** muscle and the **dilator pupillæ** muscle. The third cranial nerve supplies the sphincter and the sympathetic nerve supplies the dilator pupillæ muscle, and both nerve centers are in tonic activity so that if the sphincter pupillæ is paralysed the pupil dilates and if the dilator is paralysed the pupil contracts. Stimulation of the cervical sympathetic nerve will cause dilatation of the pupil while if the third nerve is excited it will contract.

**Action of Atropin on Pupil**—When the drug atropin is applied to the eye it paralyses the endings of the third nerve, both in the sphincter pupillæ and in the ciliary muscles, the result being that the pupil dilates because the tonic activity of the dilator center is unaffected. Also accommodation for near objects is impossible in an atropinised eye because the ciliary muscle cannot be used; only distant objects can be seen.

**Action of Physostigmin on Pupil**—This is the opposite to that of atropin since this drug excites the terminations of the third nerve and thus produces contraction of the pupil and, at the same time, accommodation for near objects by causing contraction of the ciliary muscles. An eye treated with physostigmin cannot see distant objects clearly.

**Pupillary Light Reflex**—When a BRIGHT LIGHT is thrown into the eye the PUPIL CONTRACTS, and not only the pupil of the eye into which the light falls but also that of the other eye. Put the hand up edgewise, in front of the face, to act as a partition between the two eyes, and then bring a candle before one eye; both pupils will contract. Again, stand in front of a mirror and note the size of the pupils; now close one eye and the pupil of the other eye will dilate. The REFLEX CENTER IS SITUATED IN THE MID-BRAIN; the afferent impulse enters from the retina through certain fibers of the optic nerve; this center is connected with the nucleus of the third nerve, which supplies the sphincter pupillæ muscle, and so the efferent impulse reaches the muscle by this path, that is, the third nerve.

## Visual and Color Sensation

The sensitive terminations of the retina are found in the rods and cones, and the normal stimulus for these are the waves of light which enter the eye through the pupil. The radiant energy from the sun consists of undulations in the ether and only a limited number of these undulations excite the retina. When a beam of white light is sent through a glass prism, the undulations or waves are spread out to form a spectrum. The undulations at the violet end of the spectrum have a frequency of 800 billions per second, those at the red end 400 billions per second; the ultraviolet and ultrared undulations have no power to excite the retina. Objective light is this wave motion; subjective light is the sensation which enables us to become aware of the position of the object which gives out, transmits or reflects the undulations.

The only physical difference between the ether waves is frequency of vibration and wave length. The wave lengths of light are very short. The waves at the extreme red end of the visible spectrum have a length of 760 millionths of a millimeter and those at the extreme violet end 397 millionths of a mm., while the intermediate colors have wave lengths between these extremes. Waves of a certain wave length, falling on the retina, give rise to the sensation of redness, those of shorter wave-length to a sensation of yellow, etc.; the character of the sensation depends on the wave length. When all the waves fall on the retina simultaneously, the sensation which we call white is produced.

Two theories have been advanced to explain color vision, viz.: the Young-Helmholtz or trichromic theory and the Hering theory.

**The Young Helmholtz Theory of Color Vision**—According to this theory there are three primary color sensations, viz.: **red, green,** and **violet,** corresponding to three elements or substances in the retina. Rays of light at the red end of the spectrum, that is, of a certain wave length, excite the red element strongly and the other two—green and violet—slightly, the result being a sensation of red. Rays from the middle of the spectrum excite the green element strongly, the other two only slightly, and a sensation of green results, and so for the sensation of violet. Light from the yellow part of the spectrum, for example, excites about equally the red and green elements, but only slightly the violet, and the sensation is yellow, which is therefore a mixed sensation. The light from any part of the spectrum excites all three substances or elements in unequal degrees, and on the extent to which each substance is excited will depend the resulting sensation. If all three elements are excited equally the sensation of white is produced.

**The phenomenon of color blindness** is difficult to explain on the Young-Helmholtz theory. Color blindness may be PARTIAL or COMPLETE. In complete color blindness all color sensations are absent; only the forms of objects are seen; in partial color blindness only certain colors are absent. Partial color blindness is not uncommon; it occurs in 4 per cent. of all males, and in less than 1 per cent. of females. Absence of the red and green sensations is the most common form,—**red-green color blindness. Yellow-blue color blindness** occurs but it is much less common than the red-green variety. On the Young-Helmholtz theory it is difficult to understand why red sensations and green sensations disappear together, and similarly with regard to blue and yellow. If the red substance is absent from the retina it would explain the want of red sensations, but there is no reason why the green substance should also be absent. Besides, on the Young-Helmholtz theory, violet color blindness should also exist but is never found.

In railway men and seamen, who are guided usually by red and green lights, red-green color blindness is a serious defect. It can be detected by asking the person under examination to match colored wools; if he is color blind he will make many mistakes.

**Hering's Theory of Color Sensation**—According to this theory there are six luminous sensations arranged in three pairs—**white-black,** a pair; **red-green,** a pair and **yellow-blue,** a pair. There are three visual substances in the retina, viz.: a white-black substance, a red-green substance, and a yellow-blue substance. Decomposition of the red-green substance, say, gives rise to the sensation of red, while its restitution produces a green sensation; and similarly for the black-white and yellow-blue substances. This theory explains why blindness to red and green sensations go together; it is due to the absence in the retina of the red-green substance, and yellow-blue blindness is due to the want of the **yellow-blue substance.**

It also explains the phenomenon of **complementary** after images. Any two colors are said to be complementary which together produce white light. Red is complementary to green and yellow to blue because, if the spectral colors red and green or yellow and blue be mixed in the proper proportions, white is produced. Look at a bright red light and then close the eyes; for a few seconds the red image will remain but it gradually changes to green which is the COMPLEMENTARY AFTER IMAGE. On the Hering theory this is easily explained; the red image is caused by the decomposition of the red-green substance and when the eye is closed, and the light shut out, the rebuilding up of this substance gives rise to the green sensation.

## Field of Vision

The field of vision is that part of the external world that can be seen with one eye, looking straight in front, when the other eye is closed. On account of the fact that the rays of light pass through the lens, the outer half of the field of vision corresponds to the inner half of the retina and inner half of the field to the outer half of the retina. The extent of this field, which it is important to know in diagnosing certain diseases of the eye, is obtained by the use of an instrument called a **perimeter.**

**Ophthalmoscope**—It is also important to be able to obtain a view of the retina in the living eye and this is possible by using an instrument termed the ophthalmoscope, which consists of a concave mirror with a hole in the center through which the observer looks.

# THE NERVOUS SYSTEM

## Divisions of the Nervous System

- Nervous System.
  - Cerebro-spinal
    - Brain and Spinal Cord. (Central Nervous System).
    - Cranial Nerves and Ganglia.
    - Spinal Nerves and Ganglia.
  - Autonomic
    - Sympathetic.
    - Parasympathetic.
  - Enteric
    - Auerbach's Plexus.
    - Meissner's Plexus.

## CEREBRO-SPINAL NERVOUS SYSTEM

The cerebro-spinal nervous system consists of the brain and spinal cord (central nervous system) together with the nerves which come off from them, viz.: 12 pairs from the brain (cranial nerves) and 31 pairs from the spinal cord (spinal nerves).

### Cranial Nerves

The cranial nerves are designated numerically according to the order in which they arise from the brain, from before backwards, but they are also given alternative names descriptive of their functions or of the organs and tissues which they supply.

**The Olfactory or First Cranial Nerve** arises from the olfactory bulb and passes to the olfactory area of the mucous membrane of the nose. It is the nerve of **smell** and contains **only afferent fibers.**

**The Optic or Second Cranial Nerve** is the nerve of **sight** and is also **purely sensory.** The nerve fibers when they arise from the brain on the two sides form the **optic tracts.** These decussate, partially, in the **optic chiasma** and then go on to enter the eyeballs as the **optic nerves** which terminate in the retinæ.

**The Oculo-motor or Third Cranial Nerve** arises from the **mid-brain** and supplies all the **muscles of the eyeball** except the superior oblique and the external rectus. It contains **only efferent fibers.** Paralysis of this nerve gives rise to an external squint.

**The Trochlear or Fourth Cranial Nerve** leaves the brain behind the third and passes to the **superior oblique muscle** of the eyeball. It is a **purely motor nerve.**

**The Trigeminal or Fifth Cranial Nerve,** which arises from the middle of the pons, is a **mixed nerve** containing both sensory and motor fibers. The cells of origin of the sensory fibers are situated in the **gasserian ganglion** which corresponds to the ganglion on

the posterior root of one of the spinal nerves. The **motor fibers** supply the **muscles of mastication** and the **sensory fibers** are distributed to the **skin of the face** including the eye, and the mucous membrane of the mouth and lower part of nose. The sensory branches of this nerve are often affected with neuralgia.

**The Abducens or Sixth Cranial Nerve** leaves the brain about the junction of the medulla and pons, and contains **only efferent fibers** which pass to the **external rectus muscle** of the eyeball. Paralysis of this nerve leads to an internal squint.

**The Facial or Seventh Cranial Nerve** is a **mixed nerve** like the fifth. The **sensory fibers** carry **taste** impressions from the **anterior two-thirds of the tongue,** while the **motor fibers** supply the **muscles of the face,** otherwise known as the muscles of expression. Not infrequently the seventh nerve is damaged and this leads to **Bell's paralysis;** the skin of the face on the affected side is smooth, the eye cannot be closed and the mouth is twisted to the unaffected side due to the fact that the muscle tonus on the sound side is unopposed. In whistling or smiling, the muscles of the affected side cannot be moved, while those of the other side are, and this gives a peculiar appearance to the face.

**The Auditory or Eighth Cranial Nerve** consists of two divisions—the auditory nerve proper or **nerve of hearing** coming from the **cochlea,** and the **vestibular division,** carrying impulses inwards from the **semicircular canals** to the cerebellum mainly, which enable us to maintain our **equilibrium.** There are **no efferent fibers in** the eighth nerve.

**The Glossopharyngeal or Ninth Nerve** is distributed to the **tongue and pharynx,** as the name indicates. Like the remaining three cranial nerves it takes origin from the **medulla oblongata.** It is a **mixed nerve** containing motor and sensory fibers, the former passing to the muscles of the pharynx, the latter coming from the **posterior third of the tongue** and also from the mucous membrane of the pharynx and the soft palate.

**The Vagus, Pneumogastric or Tenth Cranial Nerve** is a **mixed nerve** and has a very **wide distribution,** sending fibers, motor, sensory, secretory or inhibitory, to the heart, lungs, pharynx, larynx, gullet, stomach, intestine, liver, pancreas, spleen, kidneys, etc. The functions of the most important of these have already been considered.

**The Spinal Accessory or Eleventh Cranial Nerve** contains **only efferent fibers** which supply two important muscles of the neck and back, viz.: the **sterno-mastoid** and the **trapezius.**

**The Hypoglossal or Twelfth Cranial Nerve** is also a **purely efferent nerve** and supplies the **tongue muscles** with their motor **fibers.**

## Spinal Nerves

There are 31 pairs of nerves that come off from the spinal cord and each arises by **two roots**—the **anterior, ventral** or **efferent root** and the **posterior, dorsal** or **afferent root,** the latter having on it a swelling termed the **posterior root ganglion.** Beyond the ganglion the two roots unite to form a **mixed nerve** carrying efferent and afferent fibers to the muscles, bloodvessels, glands, skin and other sensory surfaces and structures.

## Structure of Spinal Cord

The spinal cord is continuous with the medulla oblongata, the lowest division of the brain. It lies in the spinal canal but it does not occupy the whole width of the canal nor extend throughout its whole length; its lower end is on a level with the lower border of the first lumbar vertebra. Both the brain and the spinal cord are surrounded by three membranes—the **dura mater** consisting of strong connective tissue, the **pia mater** lying next to the nerve substance and carrying many of the blood vessels that nourish the nerve tissue, and the delicate **arachnoid mater** between these two. When the membranes (or meninges) of the brain and cord are inflamed the condition is termed cerebro-spinal meningitis.

The spinal cord is cylindrical in outline but it is **not of uniform thickness** throughout its length; it shows two swellings, one in the cervical and one in the lumbar region, the **cervical and lumbar enlargements** respectively, and from these the nerve fibers arise that supply the **upper and lower limbs.** The lower end of the cord is cone shaped (the conus medullaris) and from this there passes downwards a thin filament of grey substance (the filum terminale), surrounded by the roots of the lumbar and sacral nerves, which as they lie in the spinal canal present the appearance of a horse's tail, hence called the **cauda equina.**

## Internal Structure of Cord

When a transverse section is made through the spinal cord it is seen to consist of **white matter externally** and **grey matter in the center.** The latter, which consists mainly of nerve cells and their processes, presents an appearance somewhat resembling the letter H. The projection backwards, on each side, is termed the **posterior horn** and that forwards the **anterior horn,** while the bridge of grey matter connecting the two halves of the cord, across the middle line, and through the middle of which runs the **central** canal, forms the **posterior and anterior grey commissures.** The **central canal** of the cord is continuous with cavities in the brain termed the **brain ventricles;** these, together with the central canal, are filled with **cerebro-spinal fluid** which is practically lymph.

The spinal cord is almost completely divided into two symmetrical halves by the **posterior median septum** behind and the **anterior median fissure** in front, while on the lateral aspect of each half are two shallow grooves from which the anterior and posterior nerve roots emerge.

## Grey Matter of Spinal Cord

Within the grey matter the **nerve cells** show a more or less definite grouping. Those in the **anterior horn** are **large multipolar cells** and give origin to the fibers that leave the cord through the anterior nerve roots and pass to the **striated muscles.** Another group of cells, situated at the base of the posterior horn, on its mesial aspect, is known as **Clarke's column.** The nerve fibers which arise from these cells pass into the **cerebellar tracts** and end in the cerebellum. In the lateral part of the grey matter, between the anterior and posterior horns, is a collection of nerve cells called the **intermedio-lateral group;** it is most evident in the lower cervical and upper thoracic regions. The cells in the posterior horn are small and are scattered more or less uniformly throughout the grey matter of that region, without any arrangement into distinct groups.

## White Matter of Cord

The white matter of each half of the cord, which consists of **medullated fibers,** mainly, is divided into **three columns** by the anterior and posterior nerve roots—the **posterior column** between the posterior root and horn and the posterior median septum, the **lateral column** between the anterior and posterior roots, and the **anterio column** between the anterior root and the anterior median fissure.

The nerve cells of the grey matter and the nerve fibers of the white matter are held together or supported by a variety of connective tissue, peculiar to the nervous system, termed **neuroglia.**

**Tracts of Nerve Fibers in White Columns**—The medullated nerve fibers which make up the white columns are disposed in bundles or tracts, some carrying impusles upwards from the periphery to the higher segments of the cord and to the brain, others carrying impulses downwards from the brain to the muscles, glands, bloodvessels, etc., and others still connecting segments of the cord at different levels with each other. The positions which these various tracts occupy in the spinal cord can be made out by the method of

**Wallerian or Secondary Degeneration**—We have already seen that when a nerve fiber is cut off from its cell of origin the peripheral part of the fiber undergoes degeneration; this is termed Wallerian or secondary degeneration. If the spinal cord is cut across about

its middle, all the fibers found degenerated in the upper half of the cord, i. e. above the section, will have arisen from nerve cells situated below the section; these fibers are said to undergo **ascending degeneration.** Similarly, all degenerated fibers in the lower half of the cord come off from nerve cells in the brain or cord lying above the lesion; these form the **descending tracts.** With certain reagents such as Marchi's fluid, the degenerated fibers stain differently from normal fibers, and by this means the two can be distinguished.

## Ascending Tracts

**Tract of Goll and Tract of Burdach**—The axons of the unipolar cells of the posterior root ganglia divided into two branches one of which runs outwards to the periphery, through the mixed spinal nerve, the outer inwards to the spinal cord which it enters in the posterior nerve root. This central fiber, on entering the cord, passes into the **posterior column** and soon divides into a **short descending** and a **long ascending branch;** the former turns into the grey matter one or two segments below the point of division; the latter may enter the grey matter at a higher level, or it may ascend to the medulla oblongata and end in one of two nuclei situated there.

Those ascending fibers from the **lower half of** the cord lie nearer the posterior medium septum and form the **tract or column of Goll;** they end in relation to cells situated in the **nucleus gracilis** of the medulla. Those from the **upper half** of the cord occupy the lateral part of the posterior column, forming the **tract or column of Burdach,** and end in the **nucleus cuneatus** which lies external to the nucleus gracilis.

From these two nuclei fresh fibers arise, cross the middle line in the medulla oblongata as internal arcuate fibers, and run up, on the opposite side, as the tract of the **mesial fillet** which ends in the **optic thalamus.** From the thalamus other fibers carry the impulses to the **cortex** of the cerebrum.

**Cerebellar Tracts**—Two important ascending tracts take origin from the nerve cells of **Clarke's column,** viz.: the **Dorsal Spino-Cerebellar** or **Flechsig's Tract** and the **Ventral Spino-cerebellar** or **Gowers' Tract.** The former runs upwards in the **lateral column** of the cord, at its margin, close to the ventral aspect of the posterior horn, and ends in the **middle lobe of the cerebellum;** the latter ascends, also near the surface of the cord, in front of the last mentioned tract, and, like that, ends in the **vermis of the cerebellum.** Some fibers of Gowers' tract pass to the optic thalamus.

## Descending Tracts

**Pyramid Tracts**—The most important of the descending tracts are the cortico-spinal or pyramid tracts. The fibers arise in the

large pyramidal cells (Betz cells) of the **motor cortex of the cerebrum** and pass downwards, on the same side, through the midbrain, pons, and medulla oblongata in the lower part of which they divide into **three separate bundles.** The largest of these crosses over in the **decussation of the pyramids** to the opposite side of the cord and forms the **crossed lateral pyramid tract,** situated in the lateral column in front of the posterior horn and internal to the direct spino-cerebellar tract. A few fibers which run down without crossing the middle line occupy a similar position in the lateral column of the cord, on the same side, and form the **direct lateral pyramid tract,** while a third uncrossed bundle, lying in the anterior column, present only, however, in man and the higher apes, is termed the **direct anterior pyramid tract.**

The fibers of all three tracts end in relation to the cells of the **anterior horn** which give off the motor fibers that pass out through the **anterior nerve roots** and supply the striated or **voluntary muscles,** those of the direct anterior pyramid tract crossing in the anterior white commissure of the cord. Voluntary impulses, arising from the motor areas in the cerebrum, reach the skeletal muscles through these **two superimposed systems of neurones.** Owing to the crossing of most of the sensory and motor fibers, in the lower levels of the medulla oblongata, it will be seen that the one side of the brain presides over the opposite side of the body.

**Rubro-spinal Tract**—Another descending tract arises in a group of nerve cells situated in the midbrain termed the **red nucleus** and runs down, in the lateral column of the cord, either in front of or intermingled with the crossed pyramid tract; this is termed **Monakow's bundle** or the **rubro-spinal tract.** Its fibres end in the grey matter of the cord probably forming arborisations around the motor cells of the **anterior horn.**

**Lœwenthal's Tract**—The **descending antero-lateral** or Lœwenthal's tract lies partly in the lateral and partly in the anterior column, the fibers being, to some extent, intermixed with those of Gowers' tract, another name for which is the ascending antero-lateral tract. It arises in cells situated in the midbrain, pons and medulla oblongata and ends in the grey matter of the **anterior horn.**

**Comma Tract**—Another tract which undergoes descending degeneration is found in the **posterior column** and is termed the **comma tract of Schultze.** It consists of the short descending branches which are given off by the posterior root fibers soon after they enter the cord; these end in the grey matter at lower levels.

**Proprio-spinal Fibers**—In addition to the tracts above mentioned, which either run upwards through the cord to the brain or downwards from the brain through the cord, there are fibers which take origin in the grey matter of the cord in one segment and

run upwards or downwards to end in the grey matter of another segment. These are known as **proprio-spinal fibers**; they are contained for the most part in the anterior, lateral and posterior **ground bundles** which lie next to the grey matter. They belong to the system of reflexes and serve to connect together segments of the cord at different levels.

## THE BRAIN

The brain is a very complex organ. It consists of collections of grey matter, the nerve cells of which form the brain "centers," and numerous strands of fibers (white matter) connecting these nerve centers with each other.

### Divisions of Brain

The brain is divided, more or less artificially, into five parts—the medulla oblongata, the pons, the cerebellum or little brain, the midbrain, and the cerebrum or great brain.

### The Medulla Oblongata

**The medulla oblongata,** sometimes known as the **bulb,** is the continuation of the spinal cord upwards into the cranial cavity, the edge of the foramen magnum marking the line of division between the two. The bulb is shaped like a truncated cone with the base upwards. Most of the strands of fibres that connect the spinal cord with the parts of the brain above—pons, cerebellum, midbrain and cerebrum—pass through the medulla oblongata, and besides, new tracts arise from masses of grey matter within it. The central canal of the spinal cord is continued upwards through the lower half of the medulla, gradually approaching the posterior surface, and about its middle this canal comes to the surface, the grey matter surrounding it spreading out and forming the **floor of the fourth ventricle.**

The main masses of grey matter that appear de novo in the medulla oblongata, and are not represented in the spinal cord, are the **inferior olivary nucleus,** lying postero-external to the anterior pyramid, and the **nucleus gracilis** and **nucleus cuneatus,** situated on the posterior aspect of the central grey matter. The former is connected through a strand of fibers with the lateral lobe of the cerebellum of the opposite side, while the gracile and cuneate nuclei, as we have seen, give origin to fibers that cross the middle line and form the tract of the mesial fillet which ends in the optic thalamus, a large mass of grey matter situated in the cerebrum.

The motor nuclei of the 9th, 10th, 11th, and 12th cranial nerves lie in the medulla and also most of the reflex centers already considered, viz.: the cardio-motor, cardio-inhibitory, vaso-motor, respiratory, salivary, swallowing, gastric secretion centers, etc. Be-

cause of the presence of these reflex centers, some of which are essential to life (respiratory center), a slight injury to the medulla oblongata may prove fatal.

The anterior pyramids in the upper half of the medulla forming rounded elevations at each side of the anterior median fissure in front, which is here very shallow, contain the fibers of the pyramid tract. These decussate in the lower part, the bundles interlacing as they cross the middle line.

The **restiform body** on the lateral aspect is made up of many groups of fibers, e. g. those of the direct spino-cerebellar tract already considered, that pass to the cerebellum. It is also known as the inferior cerebellar peduncle.

## Pons Varolii

**The pons varolii** is a continuation of the medulla oblongata upwards. It forms the bridge in a double sense since it connects the bulb with the midbrain and cerebrum above, and the two lateral lobes of the cerebellum with each other, through the middle cerebellar peduncles. The pyramid tract at this level is split up into separate bundles by the transverse fibers of the pons, and immediately dorsal to these lies the mesial fillet. The motor nuclei of the 5th, 6th, and 7th cranial nerves are found in the grey matter of the pons.

## Midbrain or Mesencephalon

**The midbrain** lies between the pons and the cerebrum. The **cerebral peduncles** are seen on its anterior aspect and four **corpora quadrigemina**—an anterior pair and a posterior pair—behind. When cut transversely, the **aqueduct of Sylvius** is found near the center, a canal similar to that present in the spinal cord. The aqueduct is surrounded by grey matter and serves to connect the third with the fourth ventricle. The cerebral peduncles, one on either side of the middle line, lie in front and contain the fibers of the two pyramid tracts at this level. The third and fourth cranial nerves have their nuclei of origin in the grey matter in front of the aqueduct of Sylvius, and also the superior motor nucleus of the fifth.

The motor nuclei of all the cranial nerves, in the midbrain, pons and medulla, correspond to the cells of the anterior roots of the spinal cord which give rise to the motor fibers of the efferent roots of the spinal nerves. Nerve fibers from the pyramid tract of the opposite side cross the median raphe and end in relation to the cells of each of these nuclei, so that the voluntary muscles supplied by the cranial motor nerves are controlled by the cerebral hemisphere of the opposite side.

Another important collection of nerve cells found in the midbrain is known as the **red nucleus** which, as we have seen, gives origin to the fibers of the rubro-spinal tract. The **mesial fillet** runs upwards on its way to end in the optic thalamus and during the passage of this tract through the medulla and pons, its fibers are being increased by the addition to it of the secondary neurones, related to the afferent fibers of the mixed cranial nerves.

## The Cerebrum

**The cerebrum,** in man and the higher mammals, is by far the largest and, in many respects, the most important division of the brain. It consists of two halves called the **cerebral hemispheres,** connected together across the middle line by a large flattened strand of commissural fibers termed the **corpus callosum,** at the bottom of the great longitudinal fissure which incompletely separates the hemispheres from each other.

In the interior of each hemisphere a cavity is found, filled with cerebro-spinal fluid; this is termed the **lateral** ventricle; it communicates with the third ventricle of the brain situated mesially between the two optic thalami, and that in turn, through the aqueduct of Sylvius, with the fourth ventricle into which, as we have seen, the central canal of the spinal cord opens. This whole system of canals and ventricles is filled with cerebro-spinal fluid.

**Each cerebral hemisphere,** like the other divisions of the central nervous system, consists of masses of grey matter and strands or tracts of white matter. Most of the grey matter is disposed on the surface and forms the **cerebral cortex,** while deeper down, in the base of the hemisphere, near where it joins the midbrain, are three additional masses of grey matter termed the **basal ganglia;** these are the **optic thalamus,** the **lenticular nucleus** and the **caudate nucleus,** the last two together being known as the **corpus striatum.** Between the lenticular nucleus and a depression on the surface termed the island of Reil is another collection of grey matter, flattened and elongated, known as the **claustrum.**

**Internal Capsule**—The nerve fibers which form the white matter of the hemisphere, in passing down from the cortex to the cerebral peduncles in the midbrain, converge like the lines of a fan, and most of them at the base of the hemisphere lie between the lenticular nucleus on the outside and the head of the caudate nucleus and the optic thalamus on the inside; these constitute the **internal capsule.** It is divided into an **anterior limb,** lying between the head of the caudate and the lenticular nucleus, and a **posterior limb** between the lenticular nucleus and the optic thalamus, the point of junction between the two limbs where they form a wide angle being called the **genu.** The layer of white matter between the lenticular nucleus and the claustrum is called the **external capsule.**

**Cerebral Fissures, Lobes and Convolutions**—The area of the grey matter on the surface of each hemisphere is much increased by a great number of depressions called **fissures or sulci** leading to infoldings of the cortex. The largest and deepest of these, termed the primary sulci, mark the lines of separation between the lobes into which the hemisphere is divided. The lobes are further subdivided into **convolutions or gyri** by the secondary sulci.

In mammals low in the zoological scale, such as the rabbit, the cerebral cortex is smooth, but in animals such as the cat, dog, monkey and particularly in man and the higher apes, the brain is convoluted, the advantage of this being that it permits of a large area of grey matter being accommodated in a comparatively restricted space, viz.: the cranial cavity.

On the external aspect of the hemisphere, in man, there are three primary fissures which subdivide it into five lobes, viz.: the fissure of Sylvius, the fissure of Rolando and the parieto-occipital fissure.

**The fissure of Sylvius,** at its origin near the island of Reil, divides into a short anterior and a long posterior limb, the former running into the frontal lobe and the latter separating the parietal lobe above from the tempero-sphenoidal lobe below.

**The fissure of Rolando or central fissure** begins below, near the Sylvian fissure, and runs upwards and backwards to a point near the mesial border of the hemisphere; it lies between the frontal and parietal lobes and marks the posterior boundary of the motor areas.

**The parieto-occipital fissure** separates the parietal and occipital lobes on the external aspect. It runs parallel to the Rolandic sulcus and extends over the border on to the mesial aspect of the hemisphere. The part of it that lies on the external surface is short in man, and it is usually interrupted by small connecting convolutions that are common to the parietal and occipital lobes. In the monkey, where the convolution pattern is simpler, it is better marked than in man.

**Lobes of the Cerebrum**—On the external aspect the lobes of the cerebrum are five in number, viz.: the **frontal lobe** lying in front of the Rolandic fissure; the **parietal lobe** between the Rolandic and parieto-occipital fissures and bounded below by the posterior limb of the Sylvian fissure; the **occipital lobe** behind the parieto-occipital fissure; the **temporo-sphenoidal lobe** below the posterior limb of the Slyvian fissure; and the **island of Reil,** an area of grey matter sunk beneath the level of the general surface and covered over by the convolutions that border the Sylvian fissure at the point where it divides.

**Convolutions**—Each of these lobes is further subdivided into convolutions by secondary fissures. The frontal lobe shows four well marked convolutions—ascending, upper, midle and lower

frontal convolutions; the parietal lobe contains the ascending parietal, the supramarginal, the angular and the superior parietal convolutions; the occipital lobe is divided into the upper, middle and lower occipital convolutions, and similarly the tempero-sphenoidal lobe, by two secondary sulci running parallel with the Sylvian fissure, into upper, middle and lower temporal convolutions. The island of Reil consists of a triangular shaped cluster of six more or less distinct convolutions hidden from the surface by the overlapping opercula.

On the mesial aspect of the hemisphere the fissuration is not so distinct but the following convolutions may be mentioned—the marginal convolution and the callosal convolution, above the corpus callosum, both lying in the frontal lobe and partly in the parietal; the uncinate gyrus, the cuneus and the precuneus. The calcarine fissure in the occipital lobe is well marked on this aspect.

The orbital surface of the frontal lobe, that is, the surface which rests on the orbital plate of the frontal bone, also shows three more or less distinct convolutions.

## Microscopical Structure of Cortical Grey Matter

The grey matter consists of nerve cells and nerve fibers, and of these it is possible to make out five layers, although the structure of the cortex varies somewhat at different parts.

Little is know regarding the functions of the nerve cells found in these different layers.

Nerve fibers of the white matter underlying the grey cortex may be divided into three groups, viz.: projection fibers, commissural fibers and association fibers. These run in the **corona radiata,** the term applied to the white matter of each cerebral hemisphere.

**The projection fibers** connect the cerebral cortex with the grey matter of the other divisions of the brain at lower levels and with that of the spinal cord. They are both efferent and afferent, some carrying impulses away from the cortex and others towards it. The pyramidal tract is an example of the former, where the fibers take origin in the Betz cells of the motor cortex and pass downwards, to end in relation to the cells forming the nuclei of the cranial motor nerves and in the anterior horns of the spinal cord.

**The commissural fibers,** sometimes called bilateral association fibers, pass from the convolutions of one hemisphere, across the middle line, mainly through the corpus callosum, to those of the other hemisphere.

**The association fibers,** sometimes called unilateral association fibers, connect different convolutions of the hemisphere together. Some are short, passing between two adjacent convolutions, while others are very long, extending, it may be, from the frontal to the

occipital poles. The great mass of the white matter of the cerebral hemispheres consists of these association fibers, long, short and intermediate.

### The Cerebellum

**The cerebellum** or little brain lies behind the pons and medulla oblongata. It consists of a middle lobe, termed the **vermis,** and two lateral lobes known as the **cerebellar hemispheres.**

It is composed of grey and white matter, and like the cerebrum, the main part of the grey matter lies on the surface and is known as the **cerebellar cortex.** It is highly convoluted, more so even than the cerebrum, the infoldings or fissures being deep and very numerous, thereby greatly increasing the area of grey matter. Besides this there are several collections of grey matter in the interior, the chief being the **dentate nucleus,** situated deep in each lateral lobe, and the **roof nuclei** in the vermis.

The white matter consists of nerve fibers leading into the **three pairs of peduncles** that connect this organ with the other divisions of the brain. The inferior pair of cerebellar peduncles consist of fibers leading up from the spinal cord and bulb to reach the cerebellum. The middle peduncles connect the nuclei pontis of one side with the lateral lobe of the cerebellum of the opposite side; and the superior peduncles carry fibers from the lateral lobe of the cerebellum which, through a series of relays, convey impulses to the cerebral hemisphere of the opposite side. A very important connection exists between the cerebellar cortex and the vestibular nerve which has its origin in the semicircular canals of the inner ear.

Miscroscopical sections through the cerebellum, at right angles to the surface, show the cortical grey matter of both vermis and hemispheres to consist of two more or less distinct layers, and between these are found the antler cells or **cells of Purkinje** which are characteristic of the cerebellum.

## FUNCTIONS OF THE SPINAL CORD

The functions of the spinal cord are two-fold: 1. It acts as a center (or series of centers) for the transformation of afferent impulses, received through the posterior nerve roots from the peripheral receptors, into efferent impulses transmitted through the anterior nerve roots to the effectors such as muscles and glands. This is known as **reflex action** and has already been discussed, in a general way. In man an examination of the spinal reflexes is of great importance and value to the physician in making a diagnosis in cases of nervous disease. The reflex actions obtainable from the spinal cord may be divided into three classes, from the physicians' point of view—1, superficial or skin reflexes; 2, deep or tendon reflexes; 3, visceral or organic reflexes.

## The Cord as a Center for Reflexes

**Superficial Reflexes**—When the skin of certain parts is stimulated gently, as, for example, by drawing the finger nail or a pencil point across it, certain muscles respond by contracting if the reflex arc is complete. A good example is the **plantar reflex** which consists in the withdrawal of the foot when the skin of the sole of the foot (plantar surface) is tickled. This movement is reflex and consequently involuntary, but the subject may or may not be conscious of it. The spinal center for this reflex lies in the 1st, 2d, and 3d sacral segments of the cord, the afferent path being the nerve fibers from the skin of the sole that enter by the posterior roots of the spinal nerves belonging to these segments, and the efferent path the motor nerves to the muscles of the lower limb used in withdrawing the foot. If the physician finds that this reflex cannot be elicited he concludes that the reflex arc is interrupted at some point and, if by further examination he is able to exclude the afferent and efferent factors, this indicates that the lesion exists in the grey matter of the cord, in the sacral segments above mentioned. Again, it will be remembered that in decerebrate animals, or in animals with the spinal cord cut across, the reflexes from the lower half of the cord is more easily elicited than in the normal condition, the reason being that the inhibitory impulses which are continually being showered down on the spinal cord centers from the higher brain centers are absent. If then the physician finds the plantar reflex more easily elicited than usual, or the response exaggerated, he concludes that a lesion is present in the motor paths (pyramid tracts) of the cord at a higher level.

In addition to the plantar reflex other well known reflexes are normally present in man, e. g. the gluteal reflex, the abdominal reflex, the epigastric reflex, the interscapular reflex, etc. In each case the muscles of those regions contract when the skin over them is stimulated in the way stated. The afferent and efferent nerves, and the segments of the spinal cord in which the centers for each of these reflexes lie, are known, so that a failure to bring out the particular reflex helps the physician in many cases to locate the lesion.

A well known superficial reflex, although it is not spinal, is the **conjunctival reflex** which results in the winking of the eye by the contraction of the muscle of the eyelid, viz.: the orbicularis palpebrarum, when the conjunctiva is excited. This is often used in surgical operations to determine when the patient is sufficiently under the influence of the anæsthetic; the disappearance of the reflex indicates that this stage has been reached.

**Tendon or Deep Reflexes**—The best example of a tendon reflex is the **"knee-jerk."** This is called forth when the extensor tendon,

just below the patella, is struck a sharp blow with the edge of the open hand; the foot is then suddenly and involuntarily kicked or jerked forwards. To obtain the jerk the tendon must be slightly on the stretch and this is affected by asking the subject to put one leg over the other (see diagram). The kick is caused by the sudden contraction of the quadriceps extensor group of muscles in front of the thigh. The afferent and efferent nerves are known and the center lies in the 2d and 3d lumbar segments of the cord. In diseases such as locomotor ataxia and infantile paralysis, where the reflex arc is broken (in the former case in the entering posterior root fibers and in the latter case in the grey matter of the cord), the knee-jerk is abolished, and in case of damage to the pyramid tract fibers, such as might result from a stroke of apoplexy, it is exaggerated.

Another deep reflex which is not present as a rule in the normal condition of the nervous system, but only when there is damage to the pyramid tract fibers higher up, is the **ankle-clonus.** This is obtained from stretching the tendo achilles by suddenly dorsiflexing the foot at the ankle joint (see diagram). Such flexion is followed by a series of clonic contractions of the calf muscles leading to rhythmical extension movements of the foot.

**Visceral Spinal Reflexes**—Emptying of the urinary bladder (micturition), of the rectum (defæcation) and of the uterus (parturition) may be brought about reflexly through centers for each situated in the lumbo-sacral region of the spinal cord. Each of these acts may be carried out, unconsciously of course, when the spinal cord is completely severed above the lumbar enlargement but not when the grey matter of the lumbo-sacral region is destroyed.

**Muscular Tonus**—All the muscles, whether supplied by the spinal or cranial nerves, are maintained normally in a state of semicontraction and this condition is known as **tonus.** If the motor nerve to any particular muscle be divided, or if the afferent nerve to the same segment of the cord from which the motor fibers spring be cut, then this condition of tonus is lost and the muscle remains completely and permanently relaxed. Since it is abolished by dividing the afferent nerves this tonus is reflex and is maintained normally by the continual reception of afferent impulses from the skin and other peripheral tissues.

### The Cord as a Trophic Center

The spinal cord also serves as a trophic center for the muscles and other tissues which are innervated by it. When a motor nerve is cut, for example, not only does its peripheral part undergo degeneration but also the muscle in which it terminates. The muscle fibers atrophy and shrink to less than a quarter of their size,

it may be, the transverse striation disappears and the whole muscle dwindles and decays. For this reason it is believed that there is some influence (trophic) normally exerted on the muscle, by the nerve cells in the spinal cord, whereby its nutrition is maintained, and when this is cut off the muscle degenerates. Since division of the afferent nerve will not produce this effect it is not due to the same cause as muscle tonus.

### The Spinal Cord as a Conductor

According to the **Bell-Magendie** law all the impulses that reach the spinal cord from the periphery enter through the posterior nerve roots. The fibers conveying these impulses lie in the **tracts of Goll and of Burdach,** in the posterior columns; some enter the grey matter of the cord while others, reach the medulla oblongata and terminate in the **nucleus gracilis** and **nucleus cuneatus.** The **mesial fillet** fibers arise from cells situated in these two nuclei, **cross the middle line** and end in the **optic thalamus** from which fresh fibers take origin and pass to the grey matter of **cerebral cortex.** Sensory impressions from the skin and other sensitive surfaces may reach the sensory areas of the cerebral cortex by passing over these **three superimposed systems of neurones,** viz.: periphero-bulbar, bulbo-thalamic, thalamo-cortical, and there give rise to sensations.

Another pathway to the cortex is through the **spino-thalamic fibers of Gower's tract** to the optic thalamus and by a second neurone, from there to the sensory areas of the cortex.

It will be remembered that both **dorsal** and **ventral spino-cerebellar tracts** arise in the cells of **Clarke's column,** in the grey matter of the cord, and end in the **vermis** or middle lobe of the cerebellum. Many of the fibers of the posterior nerve roots that enter the grey matter of the cord end in relation to the cells of Clarke's column, so that impulses entering the spinal cord from the periphery may reach the cerebellum through the spino-cerebellar tracts, above mentioned, and from there arrive at the cerebral cortex.

A fourth route by which impulses, coming into the cord over the posterior nerve roots, may reach the cortex is by the **proprio-spinal system** of fibers found in the **ground bundles.** These connect one segment of the cord with another, the system being continued up into the medulla, pons, and midbrain to the optic thalamus as the **posterior longitudinal bundle.** The thalamus it will be seen is a great sensory nucleus, or series of nuclei, forming the last cell station on the afferent path to the cerebral cortex.

Most of the fibers of the posterior nerve roots enter the grey matter of the spinal cord and connect, either directly or indirectly,

with cells of the anterior and lateral horns, thus forming reflex arcs, the anatomical basis for spinal reflex action.

From the above description it will be seen that afferent impulses coming in through the posterior nerve roots may reach A, the cerebral cortex, affecting consciousness and giving rise to sensations; B, the cerebellum, leading to the muscular coördination necessary to maintain bodily equilibrium; C, the grey matter of the spinal cord, giving rise to reflex action.

## Sensory Conduction

Sensory impressions of various kinds are received from the skin, and from the structures underneath it such as the muscles, and these, on reaching the spinal cord, travel up one or other of the paths described above, to reach the sensory areas of the cerebral cortex. Impulses giving rise to sensations of warmth, cold, pain, and certain forms of touch are believed to cross early in the cord and to travel up the lateral column of the opposite side, possibly through the spino-thalamic fibers of Gowers' tract, or by way of the cerebellum, to the cerebrum. The sensations arising from muscles, tendons and joints,which enable us to tell the position of a limb in space, for example, that is the sense of passive position and of movement, and the form of touch known as tactile discrimination, pass up the posterior column (tracts of Goll and Burdach) of the same side as that on which they enter and cross to the other side in the medulla oblongata, whence they reach the cerebral cortex through the mesial fillet and the thalamo-cortical fibers. **All forms of sensation ultimately cross the middle line before reaching the cerebral cortex** so that the cerebral hemispheres of one side receives its sensory impressions from the opposite side of the body; thus, damage to the sensory areas of one side of the cerebrum will result in sensory paralysis of the opposite half of the body. The **crossing is not complete,** however, for in all cases a few impressions reach the hemisphere of the same side.

## Motor Conduction

**Motor impulses,** arising in the motor areas of the cerebral cortex, are carried down the cord mainly by the **fibers of the pyramid tract.** Since most of these cross to the opposite side, in the lower region of the medulla oblongata, and run down the lateral column of the cord as the crossed lateral pyramid tract, to end either directly or indirectly, in the anterior horn, from which other fibers emerge through the anterior nerve roots, to pass to the voluntary muscles, the relationship here is also a crossed one—**one side of the cerebrum presides over the muscles of the opposite side of the body.**

Impulses travelling over this system of fibers lead to **voluntary movements**; it is called the **primary motor path** because it is

possible for voluntary impulses to reach the muscles through another route known as the **secondary motor path.** If both pyramids be divided in a dog, at the point where they decussate in the medulla oblongata, the motor paralysis which results is quickly recovered from. The reason given for the recovery is that, in the absence of the pyramid tract system, the impulses are shunted into the **rubro-spinal tract** or the **tract of Lœwenthal,** and so reach the grey matter of the spinal cord by this **secondary path,** the function of which is normally in abeyance. As we ascend the animal scale the pyramid tract system (primary motor path) becomes more and more important; it is more highly developed in the monkey than in the dog and more still in man. In man a lesion in the pyramid tract is never recovered from.

**Effects of Lesions in Spinal Cord**— Complete transverse section of the spinal cord, experimentally in animals, or extensive damage by accident or disease in man, will lead to motor and sensory paralysis on both sides below the lesion. If the interruption is in the thoracic region, so that the lower half of the body is paralysed, the condition is known as **paraplegia.** Hemisection of the cord, that is, division of one lateral half, will lead to motor paralysis below the lesion, on the same side, and sensory paralysis of the opposite side. If the pyramid tract be damaged on one side anywhere above its decussation in the medulla oblongata, muscular paralysis of the opposite side of the body will follow; this is known as **hemiplegia.** This condition is most frequently caused by the rupture of a bloodvessel near the pyramidal fibers in the internal capsule, the escaping blood tearing the fibers across or the pressure of the clot on the fibers preventing the conduction of nerve impulses through them. This is one cause of **apoplexy.** Paralysis of a single limb (arm or leg), or one side of the face, is termed **monoplegia.** This may be caused by the disease or destruction of the cells in the anterior horns of the cord, or of the motor nuclei in the brain, which send fibers to the particular parts involved.

## FUNCTIONS OF MEDULLA OBLONGATA, PONS, AND MIDBRAIN

These divisions of the brain, particularly the medulla, contain many important reflex centers such as the cardiac centers, the respiratory center, the vasomotor center, the deglutition center, the salivary center and many others. In addition to this they contain groups of cells which give origin to the efferent fibers of the cranial nerves, termed the cranial motor nuclei, which correspond to the cells of the anterior horn of the spinal cord. These nuclei receive fibers from the pyramidal tract in its passage downwards, above the decussation, which cross the middle line before reaching

the nuclei. They also contain groups of cells which serve as the terminal nuclei for the afferent fibers of the cranial nerves, resembling in this respect Clarke's column, e. g. in the grey matter of the spinal cord in relation to the fibers of the posterior nerve roots. The nerve cells of these nuclei give off fibers which cross the middle line and join the **mesial fillet,** the great sensory tract, that arises in the medulla oblongata from the **nuclei gracilis and cuneatus.** The motor and sensory conduction paths, pyramid tract and mesial fillet respectively, between the cerebrum and spinal cord, also pass through these lower divisions of the brain.

## FUNCTIONS OF CEREBRUM

The grey matter of the cerebral cortex is the seat of intelligence and of the will, since, when it is removed in the lower animals, both disappear. It is much more highly developed in man than in any of the lower animals; it is the organ of psychical activity in all animals, where it exists.

**Localization of Functions**—Until about the middle of the nineteenth century it was believed that there was no differentiation of function in the cerebral cortex, that is, every region of the grey matter was supposed to have the same function or functions.

**Speech Center**—The first discovery of any localization of function in the cerebral cortex was made by Broca, a French physician. He observed, that in certain cases of cerebral hæmorrhage, where the power of speech was lost, on post-mortem examination, the lesion was found to be located in the posterior part of the inferior frontal convolution. This is now known as **Broca's convolution** or **the speech center.** Destruction of the grey matter in this region leads to the loss of speech, although questions written or oral, are understood and can be answered in writing. This speech center is only found **on one side;** in right-handed individuals it lies in the **left hemisphere** and in left-handed individuals in the **right hemisphere.**

### Motor Areas

These were first postulated by the London physician Hughlings Jackson. He observed in certain cases of mild epilepsy (now known as Jacksonian epilepsy), where the convulsions were limited to one limb, that the movements followed a certain order or march, e. g. they would begin in the muscles of the thumb and spread to those of the fingers, forearm and upper arm. In some of these cases there was the history of injury to the skull in the region of the Rolandic fissure and Jackson argued that the irritation to this part of the cortex, by a spicule of bone, for example, is the cause of the arm movements. This is now known to be the case.

The motor areas were first demonstrated by two German physiologists, Fritsch and Hitzig. In an anæsthetized dog they exposed the cerebral cortex in the region of the crucial sulcus and stimulated it with galvanic electricity. On applying the electrodes to a certain spot in front of this sulcus they obtained **movements of the head** (by contraction of the neck muscles) to the opposite side; stimulation of another area, lateral to the first, led to **movements of the arm** on the opposite side; and similarly for the **leg area** lying behind the sulcus. The connection received further proof when it was discovered that **extirpation** of the cortical area led to **paralysis** of the muscles which had previously responded to stimulation of that area.

This work was continued by Ferrier, Horsley, Beevor, Schäfer and others, on the monkey, the final word, up to the present time, being given by Grünbaum and Sherrington on the chimpanzee, orang utang and gorilla (see diagram). The motor areas in these anthropoid apes (which probably agree closely with those in man) occupy on the lateral aspect the whole extent of the ascending frontal convolution (often called the precentral convolution) being limited behind by the fissure of Rolando or central sulcus. On the mesial aspect of the hemisphere it extends only a few millimeters over the border.

The **leg area** lies nearest the middle line and extends over the mesial border; then, in order, come the **body, arm, and neck areas** from above downwards, and lastly at the lowest extremity of the convolution comes the area which on stimulation gives movements of the **tongue, mouth and face** muscles. An area, in front of the others, and separated from the precentral convolution, is associated with **movements of the eyeballs.**

Extirpation of any one of these areas results in paralysis of the muscles which respond to its stimulation, and is followed by degeneration of the fibers of the pyramid tract which convey impulses to the segments of the brain or spinal cord which innervate these muscles. Similarly, in man, destruction of the motor areas in disease, for example by hæmorrhage or tumour, leads to paralysis of the corresponding groups of muscles and to degeneration of the fibers that take origin in the nerve cells of these areas. By the application of proper staining methods the degenerated fibers may be traced to their terminations.

### Sensory Areas

Ferrier was the first to discover the presence of sensory areas in the cerebral cortex. It is in these that the various afferent impulses from the skin, muscles and special sense organs arrive. Destruction of the peripheral organ, of any of the nerve fibers or

cells on the afferent path, or of the grey matter of the sensory area, will result in the loss of that particular sensation.

**Vision Center**—This is situated in the **occipital lobe.** Destruction of the occipital lobe, on the right side say, or of that part of the grey matter on its mesial aspect in the region of the calcarine fissure, will produce blindness in the right halves of the two retinæ. Objects in the left fields of vision will not be seen. The reason for this is that the **fibers of the optic nerves** which come from the **inner or nasal halves** of the retinæ **decussate in the optic chiasma** while those from the outer or temporal halves do not (see diagram). Extirpation or destruction of both occipital lobes results in total blindness.

**Auditory Center**—This is situated in the posterior part of the **superior temporal convolution.** If this area be removed in an animal such as a dog or a monkey, or be destroyed in man by disease, the **opposite ear is deaf.** If it be removed or destroyed on both sides total deafness follows. The connection here appears to be completely crossed.

**The Centers for Taste and Smell** have not been located with certainty. They are believed to lie in the uncinate gyrus and possibly the tip of the temporal lobe. These areas are much more highly developed in animals like the dog, where smell is the leading sense, than they are in man.

**Tactile Area**—This is believed to lie in the ascending parietal or **postcentral convolution** immediately behind the motor areas. Those impressions that reach the cortex through the posterior columns of the cord and the fillet tract, viz.: the sense of passive position and muscular movement, and of tactile discrimination, are believed to arrive in this convolution. Whether pain and temperature impressions are conducted here also is not certain.

**The Psychical Centers or Silent Areas**—When the motor and sensory areas have all been mapped out there is a large part of the surface left stimulation of which produces no apparent effect; these have, on this account, been called the silent areas and are believed to be associated with the intellectual or psychical functions of the brain. One of these regions lies in the **frontal lobe** anterior to the motor cortex, another in the **parietal lobe** and a third in the **island of Reil.** These are also known as **association centers** since impressions from the sensory areas are believed to be associated or built up into ideas in these regions. It has been shown in insane individuals that these association centers, in particular, have undergone degenerative changes.

## Sleep and Narcosis

In connection with the functions of the cerebrum the phenomena of sleep and narcosis are very interesting. During sleep the

activity of the cerebral cortex is in abeyance and consciousness is lost. In this respect the brain is no exception for probably all living tissues show periods of activity alternating with periods of rest, to some extent. The cells of the salivary glands, or pancreas, for example, following the phase of active secretion, require a period of rest in which to recuperate and to build up again the substances to be discharged later. Even the heart which never ceases to beat, during each cardiac cycle takes a short rest in the diastole, and the respiratory center is quiescent in expiration. In the case of the brain cells the period of sleep is the recuperative period in which anabolic changes predominate, whereas in the waking state katabolic changes are most in evidence.

**Functional Changes that Accompany Sleep**—The most striking accompaniment of sleep is **loss of consciousness,** but in addition to this other changes are observed. The **respirations become slower and usually deeper** and, in many cases, a mild form of Cheyne-Stokes breathing is present. Many of the **secretory glands become less active,** e. g. the salivary glands, the lachrymal glands, the kidneys and possibly the gastric glands. The **heart beats more slowly,** the **bloodvessels of the skin dilate** and the **blood pressure falls;** the **tonus** of the **skeletal muscles** is greatly **diminished,** and that the bodily **metabolism** generally is **less active** is indicated by the fact that **less $CO_2$ is excreted** than in the waking state.

**Cause of Sleep**—With regard to the cause of sleep several theories have been put forward of which three may be mentioned.

**The Neuron Theory**—All afferent impulses that reach the cerebral cortex are conducted over a series of superimposed neurons and pass across two or more synapses at which they are supposed to meet with a certain amount of resistance depending, it is assumed here, on the distance between the dendrites of the one neuron and the terminal arborisations of the other. Assuming again that the dendrites are contractile, if as a result of functional activity these slowly retract, at a certain point the distance will be too great for an impulse of ordinary strength to pass across; then the brain cortex will be protected from excitation and will go to sleep. During the resting (sleeping) period the processes gradually elongate, until physiological connection is again established, and at this point the sleeper awakes. A sufficiently powerful impulse, produced, for example, by a very loud sound, will cross the synapse at any time and awake the sleeper. Much of this theory is based on assumption, for there is no proof that the dendrites do retract under the influence of functional activity.

**Waste Products Theory**—By some the cause of sleep is held to be the **accumulation of waste products,** such as the sarcolactic acid produced in muscle, in the blood which leads to loss of excitability

or **fatigue of the brain cells;** when a certain stage is reached this results in loss of consciousness, that is, sleep. When sarcolactic acid or sodium lactate is injected into the blood it is known to induce fatigue and ultimately sleep. This would explain the well known fact that muscular exercise is one of the best soporifics; an outdoor laborer is seldom troubled with insomnia.

**Cerebral Anæmia Theory**—Some attribute the loss of cerebral activity to a diminished flow of blood to the brain. It is well know that fainting or syncope, accompanied by loss of consciousness, results immediately from a defective supply of blood to the brain, caused by stoppage or weakening of the heart's action. In animals and in human beings, where the brain has been exposed by an opening made in the skull, it is observed that in sleep the surface of the cortex becomes paler, indicating a diminished supply of blood, and also that the volume of the brain becomes less. The diminution in brain volume may be demonstrated by plethysmographic records taken on a revolving drum.

Howell explains the **onset of cerebral anæmia** which leads to sleep as follows: The **vasomotor center** in the medulla oblongata is continually receiving afferent impulses and, as a result, is in constant activity or tonus during the waking hours. By and bye this center, more particularly that part of it which presides over the skin area, begins to exhibit signs of fatigue and **loss of tone** so that the cutaneous bloodvessels dilate and more blood circulates through the skin, and it may be also through the abdominal viscera. More blood being supplied to the regions mentioned, less is available for the brain, and when a certain degree of anæmia is reached the blood supply will not be sufficient to maintain the activity of the brain cells and loss of consciousness will follow, that is, sleep. That the vasomotor center does lose tonus during sleep is proved by the general fall in blood pressure. The drowsiness that usually follows a heavy meal may be explained as due to the increased supply of blood to the digestive organs, leading to a certain degree of cerebral anæmia.

After a sufficient rest the vasomotor center will recover its tone, the bloodvessels of the skin and the splanchnic areas will become constricted, leading to a diminished supply of blood to these areas, and an increased supply to the brain, resulting in spontaneous awakening.

The chief objection that might be raised to this theory is that it is almost impossible to say whether the cerebral anæmia is the cause of sleep or sleep the cause of the cerebral anæmia.

No matter what the underlying cause of sleep is, we voluntarily assist it by retiring to a darkened and quiet room so as to cut out all visual and auditory impressions that might excite the cells of the cerebral cortex.

**Depth or Intensity of Sleep**—This is usually measured by the loudness of the sound necessary to awaken the sleeper. Using this method is it found that sleep is deepest about the end of the first hour and that from the second or third hour to the time of spontaneous awakening it is very light. It is in this period of light sleep that dreams occur, portions of the grey matter being aroused by external stimuli; the subjective result is the dream, the impressions being frequently sufficiently strong to implant themselves on the memory.

**Narcosis** is the term applied to the loss of consciousness produced by drugs such as morphine, alcohol, ether, chloroform, etc. The drug probably enters into chemical combination with the protoplasm of the nerve cells, diminishing their excitability, until they cease to be affected by outside influences. **Ether** and **chloroform** are used extensively for producing **surgical anæsthesia.** The vapor of the drug is inhaled and is absorbed by the blood in the lung capillaries; it is carried by the blood to the brain and there produces its action. The higher brain centers (inhibitory and psychical), situated in the cerebral cortex, are the first to succumb; consciousness is lost and with it the ability to feel pain, while the lower centers in the medulla oblongata (e. g. respiratory center) are still active. If the drug be pushed the lower centers are also paralysed and respiration stops; the duty of the anæsthetist is to keep the patient between the limits of unconsciousness on the one hand and of respiratory paralysis on the other.

## FUNCTIONS OF THE CEREBELLUM

The cerebellum is a large **coördinating center for muscular movements** and its main function is to **maintain body equilibrium.** Removal of the cerebellum, or of a part of it, in animals, or its destruction by disease (hæmorrhage or tumor) in the human subject, results in what is known as **cerebellar ataxia,** that is a staggering, reeling gait due to the want of coördination in the muscular movements necessary to maintain equilibrium in the act of walking or standing. The reason why a drunken man reels and staggers, on attempting to stand or walk, is that his cerebellar centers have been partially or completely paralysed by the alcohol taken.

Following removal or disease of the cerebellum there is also some loss of muscular strength and tonus but the chief result is the ataxia just described.

Unless the lesion is a very large one the symptoms are soon recovered from, other centers in the brain presumably taking on the functions of the cerebellum.

## AUTONOMIC NERVOUS SYSTEM

The autonomic nervous system consists of a chain of ganglia, situated outside the spinal canal, extending from the cervical to the coccygeal region, and known as the **sympathetic system,** and of other ganglia, mainly in the head and abdominal cavity, termed the **parasympathetic system.** The autonomic system is connected with the central nervous system by **preganglionic fibers,** which emerge from the spinal cord through the anterior nerve roots and through certain of the cranial nerves, and end in the sympathetic and parasympathetic ganglia. From these ganglia **postganglionic fibers** take origin and pass to their terminations in nonstriped muscle and secreting glands. There are thus two cell stations on the path of impulses passing over the autonomic system, one in the grey matter of the spinal cord or brain and the other in the sympathetic or parasympathetic ganglia.

The **preganglionic fibers** are **medullated** but considerably smaller than the medullated fibers of the cerebro-spinal system, while the **postganglionic fibers** are **non-medullated.**

## ENTERIC NERVOUS SYSTEM

This system consists of two plexuses (Auerbach's and Meissner's) of nerve fibers and cells situated in the wall of the alimentary canal. **Auerbach's plexus** lies between the longitudinal and circular layers of the muscular coat and **Meissner's plexus** is found in the submucous coat. They are believed to be connected with the autonomic system but they can act independently of it. Their nerve fibers end in the muscles and glands of the alimentary canal.

**THE END**